RISK ASSESSMENT OF PREVENTABLE DRUG-RELATED MORBIDITY IN OLDER PERSONS

By

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This dissertation is dedicated to my parents, James Elliott and Shirley MacKinnon. Thank you for your love, support, and examples of faith.

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Professional maturity has much in common with maturity as a person. One attribute common to both is a world view, an expectation that one thrives best by using one's power to serve something bigger than oneself. -Hepler and Strand (1990)

Completing a dissertation is one sure way to mature and grow as a person, as most people who have obtained a Doctor of Philosophy degree would agree. It is a long process, from the genesis of an initial idea for a research project, to the time the study comes to completion. The process is filled with times of intense struggle, frustration and difficulty, but also with times of excitement, learning, and finally, fulfillment. Perhaps the Apostle Paul had this in mind, when he said in the Book of Romans that "tribulation produces perseverance; and perseverance, character; and character, hope" (Romans 5:3b-4).

In completing a dissertation, there are many individuals who play key parts throughout the process. Obviously one group of individuals that deserves considerable acknowledgment is my dissertation committee. We worked together for countless hours shaping a rough research idea into a real research project. Charles D. (Doug) Hepler, my committee chair, should take a lot of credit. He proved to be an excellent mentor and hopefully I can have even a small portion of the success he has had as a researcher. He also helped me balance the dual roles of graduate student and research fellow over the past three and a half years.

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Abstract of Dissertation Presented to the Graduate School
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Chairman: Charles D. Hepler, Ph.D.
Major Department: Pharmacy Health Care Administration

This study had three primary objectives: 1) to create operational definitions of preventable drug-related morbidity (PDRM), 2) to identify patients who are at particular risk of PDRM and who may therefore benefit from comprehensive pharmaceutical care, and 3) to create a risk stratification system for PDRM based on the number of risk factors present in an individual patient. The study was conducted in two phases. In the first phase, the Delphi technique was used with a geriatric medicine expert panel to create 52 operational definitions of PDRM in older persons. Ninety-seven patients who matched these definitions were found in 3365 older persons in a Medicare managed care health plan. This was a health plan offered by the Florida Hospital Healthcare System, a provider-sponsored network with a Medicare contract, available to all Medicare beneficiaries in three counties of Central Florida. Chart abstracts from a sample of these patients were given to a panel of five pharmacists to validate the operational definitions. Overall, the two operational definitions of PDRM that were validated were found to have a sensitivity of 87.5 percent and a specificity of 73.5 percent as compared to the panel of pharmacists.

In the second phase, a prediction model was created to identify risk factors for PDRM. The dependent variable was the occurrence of a PDRM as operationally defined, and the independent variables were the hypothesized risk factors. Forward inclusion logistic regression models and factor analysis were used to identify risk factors for PDRM. Five risk factors for PDRM were identified in the final prediction model: *four or more recorded diagnoses*, *four or more prescribers*, *six or more prescription medications*, *antihypertensive drug use*, and *male gender*. A risk stratification system was developed for PDRM based on the number of risk factors present in an individual patient. Finally, patients with PDRM were shown to use significantly more healthcare resources then patients who did not experience a PDRM.

CHAPTER 1
INTRODUCTION

The Need for the Study

Older Persons and Healthcare

The special health care concerns of older persons are important factors in health care policy and research. This problem is predicted to worsen as the baby boom generation becomes older and the percentage of the total population that is elderly becomes greater. Currently, the fastest growing segment of the United States population comprises people age 85 and older. By the year 2030, 70 million people may be enrolled in Medicare, up from the current 33 million (Rhinehart, 1996).

Health care resource utilization patterns are different in older persons. This is, in part, because older persons typically have at least one chronic condition and may have multiple disease states, experience more morbidity, and have more functional limitations than younger people. Older persons consume a disproportionate share of health care resources. Forty percent of all health care expenditures are related to older persons (Fincham, 1996) and older persons account for a large percentage of all hospital stays. Thirty-eight percent of all medications are prescribed for older persons, even though older persons only make up twelve percent of the total population (Dalziel, Byszewski and Ross, 1996). Older persons, then, clearly make a significant economic impact on the healthcare system.

While the utilization of healthcare services is higher for the geriatric population, a small subset of older persons is responsible for the majority of the utilization. A study which examined the utilization patterns of continuously enrolled Medicare beneficiaries over a four year period concluded that ten percent of the population was responsible for 88 percent of the costs (McCall

and Wai, 1983). High users in the first year tended to be high users in the following years (McCall and Wai, 1983). Anderson and Knickman (1984) studied the temporal patterns of Medicare beneficiaries' medical expenditures and concluded that unusually high expenditures for a specific person in one year allow a good prediction of high expenditures in following years. Therefore, this subset of older persons consistently uses more health care resources year after year.

Drug-Related Morbidity and Mortality

While medications are prescribed to millions of older persons in an attempt to improve their health-related quality of life, often an optimum outcome from these medications will not be achieved. A drug-related problem (DRP) is any patient and time-specific event or situation involving the medication regimen that interferes with the achievement of an optimum outcome (Hepler and Strand, 1990). Eight types of DRPs have been described (Hepler and Strand, 1990; Strand et al., 1990):

1. Untreated indication: The patient has a medical problem that required drug therapy (an indication for drug use), but is not receiving a drug for that indication.
2. Improper drug selection: The patient has a drug indication but is taking the wrong drug.
3. Sub-therapeutic dosage: The patient has a medical problem that is being treated with too little of the correct drug.
4. Failure to receive drugs: The patient has a medical problem that is the result of his or her not receiving a drug (e.g.; for pharmaceutical, psychological, sociological, or economic reasons).
5. Over-dosage: The patient has a medical problem that is being treated with too much of the correct drug (toxicity).

6. Adverse drug reactions: The patient has a medical problem that is the result of an adverse drug reaction or adverse effect.
7. Drug interactions: The patient has a medical problem that is the result of a drug-drug, drug-food, or drug-laboratory interaction.
8. Drug use without indication: The patient is taking a drug for no medically valid indication.

DRPs may lead to drug-related morbidity, which is the failure of a therapeutic agent to produce the intended therapeutic outcome (therapeutic malfunction or miscarriage) (Hepler and Strand, 1990). The drug-related morbidity results from either (a) the production of an adverse or toxic effect or (b) the failure to produce the desired effect within a reasonable time.

If the DRP is unrecognized or unresolved, then drug-related mortality can occur. Recent literature reports that the clinical, economic, and humanistic outcomes of drug-related morbidity and mortality are substantial. Lazarou, Pomeranz and Corey (1998) conducted a meta-analysis of prospective studies involving drug-related morbidity and mortality and concluded that the overall incidence of serious drug-related morbidity is 6.7 percent and the incidence of drug-related mortality is 0.32 percent. This estimate places drug-related morbidity and mortality between the fourth and sixth top cause of death (Lazarou, Pomeranz and Corey 1998). The real incidence may actually be higher, as their meta-analysis did not include drug-related morbidity due to noncompliance, drug administration errors, drug abuse, poisonings or therapeutic failures. Phillips, Christfeld and Glynn (1998) reported that this problem is growing, as between 1983 and 1993, drug-related mortality increased by 257 percent.

Preventable Drug-Related Morbidity and Mortality

Some drug-related morbidities are not preventable, including those resulting from patient idiosyncracy, while others are preventable. As described by Hepler and Strand (1990), preventable drug-related morbidity (PRDM) has four unique elements. Given an adverse clinical

outcome, a pre-existing DRP must have been recognizable and the adverse outcome or treatment failure must have been foreseeable. In addition, the causes of the DRP and the outcome must have been both identifiable and controllable. However, there are no published criteria to help determine what drug-related morbidities are, and are not, preventable. Schumock and Thorton (1992) have attempted to develop such criteria for adverse drug reactions (one type of DRP). Although their criteria are primarily drug-oriented, a similar patient-oriented approach for drug-related morbidity may be possible. Others have used these criteria successfully to determine whether adverse drug reactions were preventable (Pearson et al., 1994).

The extent of the problem of PDRM was not known until recently. A recent estimate of the total annual cost of drug-related morbidity and mortality in the ambulatory setting in the United States by Johnson and Bootman (1995) is $76 billion, with a range from $30.1 to $136.8 billion, in their cost-of-illness model. Although they used the opinions of experts and not actual utilization data to obtain this estimate, this figure is quite comparable with the costs of other major diseases, such as asthma and diabetes. Schneider et al. (1995) concluded that the annual cost to one academic medical center was approximately $1.5 million. Nelson and Talbert (1996) reported that 16.2 percent of admissions in 452 consecutive patients were due to drug-related morbidity, and 49.3 percent of these admissions were definitely preventable. Fifty-six percent of all drug-related hospital admissions in older persons in a study in Denmark were judged to have been "definitely" or "probably" avoidable (Hallas et al., 1991). Therefore, it appears that PDRM is a serious problem, especially in older persons.

Often the problem of drug-related morbidity and mortality is under-reported and underestimated. Nelson and Talbert (1996) concluded that the discharge summary of almost 20 percent of patients with a drug-related admission made no mention of this fact. They and others have lamented that there have been no rigorous methods for identifying and evaluating drug-related morbidity and mortality. Underestimation of drug-related morbidity is especially prevalent among community-living older adults, where (1) they may fail to recognize the

symptoms of drug-related morbidity or (2) their clinicians may attribute these symptoms to aging, rather than to the drugs (French, 1996).

Problem Statement

As indicated by the previous discussion, the problem of PDRM in older persons has been long recognized. The literature continues to grow with new studies of problem drugs and new estimates of the extent of the problem. Despite this, little quantitative information is known about the factors associated with increased risk that an older person would experience PDRM, especially in the ambulatory setting. A better understanding of this relationship may help to create more effective intervention strategies and more efficient use of scarce healthcare resources.

Study Objectives

There are three primary research objectives of this proposed study. These objectives are

1. To create operational definitions of PDRM,
2. To identify patients who are at particular risk of PDRM (as defined) and who may therefore benefit from comprehensive pharmaceutical care, and
3. To create a risk stratification system for PDRM based on the number of risk factors present in an individual patient.

Rationale and Theoretical Introduction

The rationale for this study will be two related models that are based on systems theory. These two models are the medication use (pharmaceutical care) system and the biopsychosocial model of disease etiology and therapy. The use of risk factors is the final important aspect of this study.

The first of these two models the medication use system. Pharmaceutical care has been defined by Hepler and Strand (1990) as being the cooperative, responsible provision of drug therapy to achieve definite outcomes intended to improve a patient's quality of life. Pharmaceutical care is quite different from our current approach to medications use.

> Pharmaceutical care differs from traditional drug treatment because . . . it is an explicitly outcome-oriented, cooperative, systematic approach to providing drug therapy, directed not only at clinical outcomes but also activities of daily life and other dimensions of health-related quality of life. Preventing, detecting and resolving pharmacotherapeutic problems before they become adverse outcomes increases the effectiveness of drug therapy. (Hepler and Grainger-Rousseau, 1995, p.8)

The development of a predictive model for PDRM in older persons may support prospective prevention of adverse outcomes related to drug therapy.

The usual medication use process is far from the ideal pharmaceutical care system. This process has been previously described (Hepler and Grainger-Rousseau, 1995). Communication and cooperation between the patient, physician, and pharmacists may be unsystematic and ineffective. The patient may develop a drug-related problem, which, if left unresolved, may develop into drug-related morbidity or even mortality. However, no one may recognize the problem or attribute it to drug therapy. This flow of care is described as a process, and not a system, because there is no feedback loop after the patient receives the prescription.

Compared to a drug therapy process, a pharmaceutical care system emphasizes the prevention, detection, and resolution of drug-related problems before they can become drug-related morbidities. To do this, a pharmaceutical care system emphasizes monitoring of patients-in-therapy to detect problems. Monitoring, in turn, increases communication among the patient, physician, and pharmacist. All three parties need more information (more often) from each other, not only to detect problems but also to prevent and resolve them.

A second dimension of the conceptual framework of this research is the biopsychosocial model. According to this model, which is also based on systems theory, many clinical outcomes, including those of drug therapy, result in part from complex interactions of psychological and

sociological factors. These factors are in addition to the physiological and chemical explanations provided in the biomedical view. Therefore, it may be possible to identify risk factors for PDRM from among a wider variety of variables than would be predicted by reasoning from the biomedical model. Furthermore, this model views illness as being more continuous and less episodic than the biomedical model and therefore it may be possibly more descriptive of the medical problems of older persons.

The third dimension of the conceptual framework of this study is the use of risk factors. Risk factors in this study are those variables that are statistically associated with PDRM (the outcome event) in older persons. While general risk factors for PDRM will be identified for an entire geriatric population, the constructed model should be applied on a patient-specific basis. This approach follows the similar use of probability theories and the rationale behind screening tests, although this study is not a classical epidemiological study. These tests use population-based information to identify the risk factors, but then the information is applied on an individual basis to identify those patients who might be at particular risk for problems. Risk factors may be used to help allocate scarce healthcare resources and as potential indicators to identify patients who need interventions. Careful consideration of these risk factors should be incorporated into the therapeutic and monitoring plans of health care professionals in order to proactively prevent PDRM in older persons. A goal of identifying older persons at risk for PDRM is to intervene in their medical care before they experience a PDRM. Risk factors are patient characteristics and therefore they may or may not be able to be changed (e.g.; it may be hard to change a patient's gender or drug therapy if it is essential). If a risk factor can not be eliminated in an individual, then at least prospective management of that risk factor should occur. This study describes an approach to use population-based information to construct a model for PDRM in older persons that will be applied on a patient-specific basis.

Research Questions

To achieve the purpose of this study, four research questions will be investigated. These questions will explore different aspects of risk factor identification of PDRM in older persons.

Research Question 1

What are the issues in developing and using operational definitions of PDRM?

Research Question 2

What are major risk factors for PDRM in older persons?

Research Question 3

Are there general, and disease (or drug), specific risk factors for PDRM in older persons?

Research Question 4

What is the relationship between PDRM and the utilization of healthcare resources?

CHAPTER 2
CONCEPTUAL FRAMEWORK

The conceptual framework for this study consists of two models that incorporate systems theory. These two models are the medication use (pharmaceutical care) system and the biopsychosocial model of disease etiology and therapy. The concept of risk factors is a third fundamental component of this study. Brief descriptions and empirical findings of these models will be discussed.

Systems Theory and the Medication Use System

Medication use can be described as a process. In general, model patients enter the health care system when they recognize a health problem and see a physician. The physician then diagnoses the patient's problem and constructs a therapeutic plan, which is often accompanied by a prescription. The therapeutic plan is implemented when the patient goes to a pharmacy and a pharmacist dispenses the prescription and provides advice about the use of the medication. The typical medication use process is completed when the patient consumes the medication. Unintended outcomes of this process include drug-related problems, which, left unresolved or undetected, may lead to drug-related morbidity. As discussed in chapter one, there are many such unintended adverse outcomes from the current medication use process and several authors have argued that this current process must be changed (Shane, 1992; Smith and Benderev, 1991).

In contrast, a medication use system emphasizes systematic monitoring and communication. This model of medication use has been described as being a philosophy of practice for pharmacists and its knowledge base is formed from systems theory (Hepler, 1996). The structure of this model is seen in Figure 2.1. Patient "progress" is monitored to prevent,

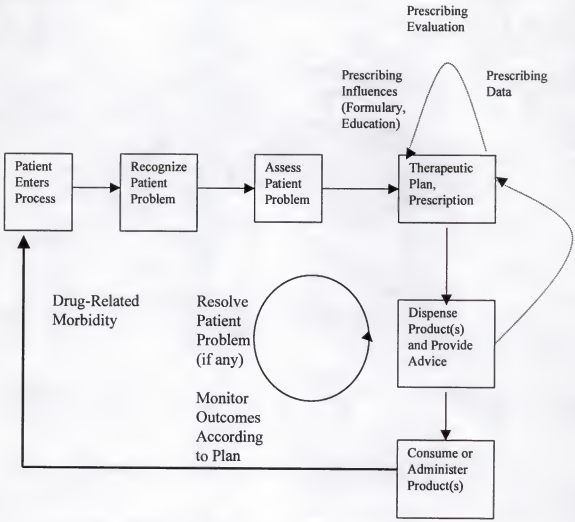


Figure 2.1 The Medication Use System

(Adopted from Hepler and Grainger-Rousseau, 1995)

detect, and resolve DRPs before they develop into drug-related morbidities. Communication between the physician, patient, pharmacist, and other health care professionals is critical to proper functioning of the system. Prevention is important, especially in older persons, since DRPs occur frequently and affect clinical, psychosocial, and economic outcomes. The medication use system has a goal of patient-care outcomes, rather than performance of tasks, as in the medication use process (Smith and Benderev, 1991).

Systems theory is the foundation upon which the medication use system is built. The phrase "systems theory" may be deceptive, as according to some definitions, it is really a model and not a theory (Babbie, 1983). Laszlo (1973) refers to systems theory as a philosophy. Regardless, at the fundamental level, systems theory, or systems thinking, is a body of knowledge that has gradually developed over the past fifty years into a model, which helps one to see and influence things from a different, larger perspective (Senge, 1994). Key to systems theory is the word *systems* itself. It is frequently used but infrequently understood. A system can be defined as follows:

> Basically, a system is (1) a group of related entities that (2) does something – receives inputs, affects them in some way, and produces outputs to achieve some purpose. Almost anything in the world can be called a system. A sheep can be considered a system. It takes in fodder and produces wool and lamb chops. (Nadler and Hibino, 1994, pp.198-199)

It is clear from this definition that one of the tenets central to systems theory is seeing the "big picture" and "whole structures". Senge (1994) states that systems theory is a method to (1) see wholes, (2) interrelationships rather than things, and (3) patterns of change rather than single elements. Nadler and Hibino (1994) call this the "systems principle": each problem is just a piece of a larger system. Many authors argue that these patterns, or structures, underlie complex situations (Senge, 1994; Nadler and Hibino, 1994; Laszlo, 1973). By learning to recognize and see them, the way by which one approaches problems will be modified. Senge (1994) elaborates on these "structures":

> one of the most important, and potentially most empowering, insights to come from the young field of systems thinking is that certain patterns of structure recur again and again.

> These 'systems archetypes' or 'generic structures' embody the key to learning to see structures in our personal and organizational lives. The systems archetypes – of which there are only a relatively small number – suggest that not all…problems are unique. (Senge, 1994, p.94)

These structures, then, are an important concept in systems theory and allow one to view problems with a larger perspective.

The medication use system has built upon many of the central principles of systems theory. These include the interrelationship of the various elements and dimensions of the medication use system, the importance of communication and feedback loops, identification of key areas of change, and the individualization of drug therapy goals and monitoring for specific patients. Systems theory also emphasizes that the medication use system can be viewed as being a subset of a larger system – the health care system – or subsets of the medication use system can be thought of systems in their own right. For example, the act of a physician writing a prescription for a patient is a complex system that has been extensively studied. The physician uses multiple inputs when deciding which drug to prescribe, such as the price of the prescription, the condition of the patient, the information given to him by a pharmaceutical representative, whether the drug is in his evoked set, and other factors. Similarly, there are many outputs and feedback mechanisms after he/she has written the prescription, such as whether the patient has improved, drug use evaluation, and any adverse effects experienced by the patient. One way of viewing these aspects of the medication use system is through the use of the system matrix.

The System Matrix Applied to the Medication Use System

While it is useful to recognize that structures exist, the size of most systems could quickly cause one to become overwhelmed by the amount of information in these structures. One way of organizing this information is to use a method called the system matrix (Nadler and Hibino, 1994). According to the system matrix, a system consists of elements and dimensions. The elements of a system are (1) purpose (the mission, aim, need, primary concern, or results sought from a system), (2) inputs (physical items, information or human beings on which work,

conversion, or processing takes place), (3) outputs (desired and undesired physical items, information, humans and services that result from processing inputs), (4) sequence (the conversion, work, process, or transformation by which the inputs become the outputs), (5) environment (the physical and sociological factors within which the other factors operate), (6) human agents (those who aid in the steps of the sequence without becoming part of the outputs), (7) physical catalysts (resources that aid in the steps of the sequence without becoming part of the outputs), and (8) information aids (include knowledge and data resources that help in the steps of the sequence without becoming part of the outputs) (Nadler and Hibino, 1994). Dimensions help clarify the conditions for each element in a specific situation (Nadler and Hibino, 1994). The dimensions of a system are (1) fundamentals (tangible, overt, observable, physical, or basic structural characteristics), (2) values and goals (motivating beliefs, human expectations, global desires, ethics, equity, and moral concerns that can be ascribed in some form to each element, (3) measures (translate the fundamentals and values dimensions into particular performance factors and operational objectives), (4) control (comprises methods for ensuring that the fundamentals, measures, and even value specifications, are maintained as desired during the operation of the system), (6) interface (the relationships of the fundamentals, values, measures, and control specifications to other elements and to external systems), and (7) future (changes in each specification of the other dimensions in the future) (Nadler and Hibino, 1994). A system matrix clearly delineates the relationships of elements and their interdependences and, most importantly according to Nadler and Hibino (1994), it prevents the omission of critical components of the system.

The system matrix can be used to describe the medication use system. As previously discussed, a system matrix helps to view a system by listing the elements and dimensions of that system. Chiefly, this allows one to see the structure of a system; in this case, the medication use system by specifying each element and dimension cell in the system matrix. For example, the

fundamentals (one of the dimensions of a system) have been previously described by Grainger-Rousseau et al. (1997). As seen in Table 2.1, these eight fundamentals, or necessities, must be present to ensure that drug therapy will be safe, effective, and humane (Grainger-Rousseau et al., 1997). The human agents (one of the elements of a system) can be described for these eight fundamentals for the medication use system. In the medication use system, the main human agents are the prescriber, the pharmacist, and the patient (and caregiver). Table 2.2 shows how each of the eight fundamentals of a safe and effective medication use system relates to these three human agents. The boxes with checkmarks indicate an important relationship between an element and a dimension. For example, fundamental one (timely recognition of signs and symptoms) often depends on the action of the prescriber, pharmacist, or patient/caregiver. This example shows how the system matrix can be applied to one cell for the medication use system.

Feedback and Communication Loops in the Medication Use System

An important concept in systems theory is feedback, also referred as communication loops. Feedback is defined by Senge (1994) as being a broad concept meaning any reciprocal flow of influence, and every influence acts as both a cause and an effect. Senge (1994) continues,

> The practice of systems thinking starts with understanding a simple concept called 'feedback' that shows how actions can reinforce or counteract (balance) each other. It builds to learning to recognize types of 'structures' that recur again and again: the arms race is a generic or archetypal pattern of escalation, at its heart no different from turf warfare between two street gangs, the demise of a marriage, or the advertising battles of two consumer goods companies fighting for market share. (Senge, 1994, p.73)

Two types of feedback have been described. The first type is reinforcing (also called amplifying or positive) feedback which causes growth. The second type is balancing (also called stabilizing or negative) feedback which counteracts the reinforcing feedback. These feedback cycles or communication loops often may have "delays", in which the flow of influence is interrupted, resulting in a slowing down of events (Senge, 1994).

Table 2.1 Eight Fundamentals (Necessities) for Safe and Effective Drug Therapy (Adopted from Grainger-Rousseau et al., 1997)

1. *Timely recognition of drug indications and other signs and symptoms relevant to drug use with accurate identification of underlying disease.* "Correct" therapy for a late or incorrect diagnosis cannot improve a patient's quality of life.
2. *Safe, accessible, and cost-effective medicines.* Safe and cost-effective (efficient) drug products must be legally and financially available.
3. *Appropriate prescribing for explicit (clear, measurable, and communicable) objectives.* Explicit therapeutic objectives simplify the assessment of prescribing appropriateness and are necessary for assessing (monitoring) therapeutic outcomes.
4. *Drug product distribution, dispensing, and administration with appropriate patient advice.* Including: (a) ensuring that a patient actually obtained the medicine, (b) negotiating a regimen that the patient can tolerate and afford, (c) ensuring that a patient (or caregiver) can correctly use the medicine and administration devices, (d) advising to empower the patient or caregiver to cooperate in his or her own care as much as possible.
5. *Patient participation in care (intelligent adherence).* The ambulatory patient or caregiver should consent to therapeutic objectives and know the signs of therapeutic success, side effects and toxicities; when to expect them; and what to do if they appear.
6. *Monitoring (problem detection and resolution).* Many failures can be detected while they are still problems and before they become adverse outcomes or treatment failures.
7. *Documentation and communication of information and decisions.* Communication and documentation are necessary for cooperation in a system.
8. *Product and system performance evaluation and improvement.* Practice guidelines, performance indicators, and databases are a useful approach to achieving and maintaining improved system performance (outcomes).

Table 2.2 The Fundamentals/Human Agents Cell of the System Matrix Applied to the Medication Use System

Fundamental for safe and effective drug therapy	Human Agents of the Medication Use System		
	Prescriber	Pharmacist	Patient/ Caregiver
Timely recognition of signs and symptoms	✓	✓	✓
Safe, accessible, and cost-effective medicines			
Appropriate prescribing	✓		
Distribution, dispensing, administration , and patient advice		✓	✓
Patient participation			✓
Monitoring	✓	✓	✓
Documentation and communication	✓	✓	✓
System evaluation			

The acknowledgement of the importance of feedback in systems theory allows one to accurately discern the role of individuals in a system. In systems theory, individuals are seen as simply part of the feedback process, and not as a separate component of a system. Individuals can act as either reinforcing or balancing feedback. This is different from the common perception that individuals are somehow special and are different from the other elements of a system. Senge (1994) notes that considering individuals as a form of feedback implies that an individual is usually not solely responsible for an action, but that everyone shares in the responsibility for the event occurring. Individuals may have different levels of influence but most systems problems are solved by looking at all the types of feedback.

Several feedback loops occur in the medication use system. As seen in Figure 2.2, there is a feedback loop for aggregated prescribing that includes prescribing data, prescribing (drug use) evaluation, and prescribing influences such as a formulary and education. A second feedback loop exists for a single patient's prescription or drug regimen. This is when information obtained by a pharmacist or another health care professional from the patient can be used to alter the therapeutic plan. A third feedback loop, which is not formalized in the medication use process, involves monitoring the patient for drug-related problems, resolving any problems which exist, and using this information to revise the therapeutic plan as appropriate.

The medication use system contains feedback loops that are reinforcing and it may also contain delays. Patient monitoring by the pharmacist can be used to reinforce or strengthen the therapeutic plan. Monitoring includes the determination of which information to collect for the evaluation of the progress of therapy, the evaluation of achieving the therapeutic objectives, and responding to evaluations (Grainger-Rousseau et al., 1997). This constant, critical re-evaluation of the therapeutic plan is an important reinforcing feedback loop that helps facilitate the provision of pharmaceutical care (Strand et al., 1991). Delays can occur at many places in the medication use system, such as when pharmacists or patients do not provide timely data to the physician, such that the therapeutic plan is not revised and poor patient care results.

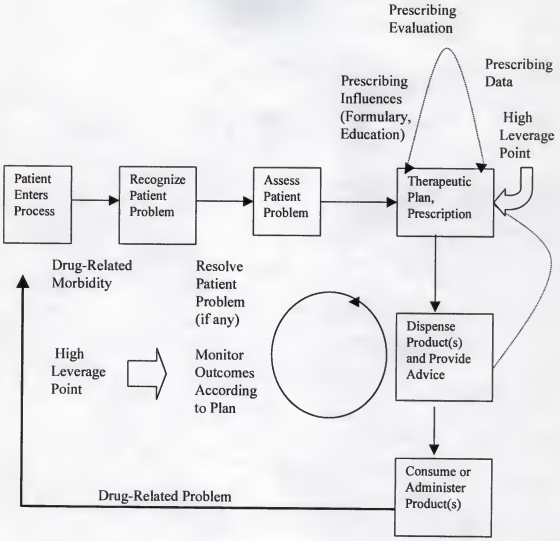


Figure 2.2 High Leverage Points Within the Medication Use System
(Adopted from Hepler and Grainger-Rousseau, 1995)

Change and the Medication Use System

The next logical step is to ask how one can influence and change the various types of feedback that exist in a given system. This skill of knowing where to affect a system to produce the greatest possible intended effect is known as leverage. Senge (1994) explains this concept,

> The bottom line of systems thinking is leverage – seeing where actions and changes in structures can lead to significant, enduring improvements…our nonsystemic ways of thinking are so damaging specifically because they consistently lead us to focus on low-leverage changes: we focus on symptoms where the stress is greatest. We repair or ameliorate the symptoms. But such efforts only make matters better in the short run, at best, and worse in the long run. (Senge, 1994, p.114)

In order to change systems the most effectively, then, high-leverage changes should be sought. By recognizing which feedback mechanisms result in the high-leverage changes, one can target those feedback points and obtain the intended effect.

In order to most effectively change the medication use system such that PDRM is minimized, high leverage change points must be identified and successful intervention strategies must be implemented. Two such high leverage points for the prevention of PDRM within the medication use system are identified in Figure 2.2: the therapeutic plan and patient monitoring. The creation and re-evaluation of the therapeutic plan is a key point in the medication use process. Without a therapeutic plan that includes explicit, realistic objectives, therapy management is practically impossible (Hepler and Grainger-Rousseau, 1995). Also, the patient risks for PDRM are generally unknown during the formation of the therapeutic plan (Strand et al., 1991):

> It seems evident that we have accumulated very little hard information that describes pharmaceutical-care needs, patient risks related to pharmacotherapy, and the drug-related problems present. Before the concept of … pharmaceutical care can be developed any further, this information needs to be collected and evaluated. (Strand et al., 1991, p.550)

Some medications, such as digoxin, have been identified in the literature as being commonly prescribed inappropriately in the older population (Aronow, 1996). There is also some evidence

that those medications that are prescribed inappropriately lead to PDRM in older adults. French (1996) argues that up to 25 percent of community-living older persons are at risk for drug-related morbidity due to inappropriate prescribing, a key part of the therapeutic plan. Ideally, a method that could prospectively identify these high-risk medications, and incorporate this information into the therapeutic plans for them, would be of tremendous value.

The monitoring and management of patient outcomes according to the therapeutic plan is a second key point in the medication use process. As early as 1981, (Campbell, 1981) an advisory committee on pharmaceutical needs in older persons recommended that identification of toxic drug effects and drug monitoring be priority functions of the pharmacist. In 1988, Grymonpre et al. (1988) stated that their study on drug-related adverse patient events confirmed the need for increased caution and monitoring of all consequences and outcomes of medication use in older persons. More recently, Johnson and Bootman (1995) recommended that urgent attention be given to this problem and monitoring should be emphasized to help lessen PDRM. Patient monitoring is also required to ensure that the desired patient outcomes and goals are attained (Strand et al., 1991; McDonough, 1996). Identification of medications for which monitoring is extremely important may greatly assist the pharmacist during patient monitoring and management to prevent PDRM in older persons.

Biopsychosocial Model of Disease Etiology and Therapy

The previous discussions on (1) the importance of feedback and communication within the medication use system, and (2) the high leverage points (the therapeutic plan and patient monitoring), show the importance of accounting for individual patient differences. As well, as was seen in Table 2.2, many of the fundamentals of safe and effective drug therapy rely on the cooperative actions of the prescriber, pharmacist, and patient. This holistic, individualized approach to medication use is complimented by the biopsychosocial model of disease etiology and therapy.

The biopsychosocial model was first proposed by Engel (1977), in response to the biomedical model. The biomedical model of disease had molecular biology as its basic scientific discipline (Engel, 1977) and tried to explain disease as being deviations from 'norms'-measurable biological variables (DiMatteo, 1991). Engel (1977, 1981) argued that such a model did not consider the person as a whole, and failed to incorporate psychological, social or behavioral aspects of illness.

Engel turned to nature, and biology in particular, for an alternative. The knowledge base from which the biopsychosocial model is built upon is the use of systems theory in biology (Engel, 1981; Sadler and Hulgus, 1992). Engel (1981) describes this foundation,

> systems theory, by providing a conceptual framework within which both organized wholes and component parts can be studied, overcomes this centuries-old limitation and broadens the range of the scientific method to the study of life and living systems, including health and illness (Engel, 1981, p.103)

and,

> systems theory is best approached through the common sense observation that nature is a hierarchically arranged continuum, with its more complex larger units being superordinate to the less complex smaller units. (Engel, 1981, pp.103-104)

As previously discussed, systems theory emphasizes this hierarchy and views each component of the system, whether it be a person or the biosphere, as not existing in isolation, but being influenced by its environment. A bee, for example, can not truly be studied without studying its environment (flowers, other bees, honeycomb, etc.). Systems theory, then, was useful to help explain how things are ordered in nature and how these different "systems" in nature interacted.

Engel advocated taking this knowledge base of systems theory in biology and applying it to the medical care of individuals, as well as medical research and teaching. This would allow for a holistic evaluation of patients – considering cultural, social, psychological, and behavioral dimensions of illness (DiMatteo, 1991), humane, empathic and rigorous medical care (Sadler and Hulgus, 1992), and patient-centered and patient-specific medical care (Howell, 1992;

Zimmermann and Tansella, 1996). This is especially important in older persons, where medical information and diagnosis are insufficient in predicting their health care needs and consideration of these other dimensions are critical (Rock et al., 1996).

This distinction between the biomedical and biopsychosocial models can be seen in the medication use system. Traditional drug treatment follows a population-based approach to care, whereas a pharmaceutical care system follows a patient-based approach. In order to improve the medications use process, the current approach utilizes population-based methods such as drug formularies and drug use evaluation. These methods follow a biomedical model of disease, whereby the disease becomes the emphasis and a mechanistic, reductionistic, and dualistic perspective is employed. Patients who have illness must be deviating from objective somatic norms and thus there is always a drug of choice that can be chosen for a whole population.

In contrast, a biopsychosocial model approach states that deviation from the somatic norm is insufficient to explain disease, and biological relationships to illness are complex interactions with the mind and environment. This model accounts for patient-specific differences in illness because it holds a monistic perspective that states the mind and body are intimately related. While a population basis can be employed to change a system, the biopsychosocial requires that individual patient differences be considered. Variation between patients is expected and is not necessarily negative. It even allows for patient disagreement with the health professional's plan of care (Kasahara, Shemon and Holzschuh, 1994). This model incorporates psychological aspects of illness (such as anxiety or depression), the individual's cultural expectations about illness, and the present social context of the illness as well as the biological parameters (DiMatteo, 1991).

The biopsychosocial model fits well with the approach to be used in this proposed investigation of PDRM in older persons, which will consider these other dimensions of illness. First, illness presentation in older persons is different from other age groups and this raises some

unique concerns. One of these unique factors is that many older persons have atypical disease presentations that do not fit a classic disease model. Jarrett et al. (1995) concluded that atypical disease presentation is associated with adverse hospital outcomes. This makes the issues of disease diagnosis and treatment far more complex in older persons and further strengthens the need to account for patient differences. Second, PDRM has been reported and analyzed on a patient-specific basis. Third, drug-related morbidity often has atypical or paradoxical manifestations in older persons (French, 1996; Harper, Newton and Walsh, 1989). This may be because patient-specific differences play a large role in the development of drug-related morbidity and mortality. Gurwitz and Avorn (1991) state that patient-specific physiologic and functional patient characteristics, such as pharmacokinetic and pharmacodynamic changes, are often very important to predict drug-related morbidity in older persons due to the inter-individual variability of the aging process. As Strand et al. (1991) explain,

> each patient must receive individualized treatment not only because of information derived from scientific knowledge but also because he or she must be consistently respected as a unique individual with specific needs. (Strand et al., 1991, p.549)

The biopsychosocial model allows for the inclusion of social, psychological, and behavioral factors in a prediction model of PDRM in older persons. This includes such things as trouble paying for medications, difficulty taking medications, patient belief that he/she is on too many medications, and the patient's own perception of their health. This is important, as, for example, an older person's self-assessment of their health as being poor has been shown to be associated with mortality in a study of recipients of community-based long-term care (Fried, Pollack, and Tinetti, 1998). A prediction model that includes this and other social, psychological, and behavioral factors may be the best way to identify PDRM in older persons.

Risk Factors for PDRM

The medication use system emphasizes an individualized approach to care. However, population-based information can be useful in planning for a specific patient. One such type of population-based information is risk factors. Risk factors are variables that are statistically associated with an outcome event. Prediction models use risk factors identified from a population and apply this information to the individual patient. The individual patient is then told the probability, or risk, of having a certain disease or medical condition.

Probability theory and its applications play a central role in the development and function of screening tests and risk factors. Medical tests results are rarely positive or negative, instead they lie on a continuum; test results that are beyond a cutoff threshold are called positive. This cutoff threshold separates the two separate, but usually overlapping Gaussian distributions of patients with, and without, the disease (condition). This relates to the concepts of sensitivity and specificity. Sensitivity is the percentage of patients with a disease (condition) who are labeled "positive" by the test, whereas specificity is the percentage of patients without the disease who are labeled "negative" by the test. A test or prediction model with a high specificity and sensitivity will have a low rate of false negatives and false positives.

Risk factor identification is an important issue, but equally important is the actual use of these risk factors in an assessment or screening program. Risk assessment generally involves a prospective investigation of a person's health risks to facilitate interventions before the occurrence of a preventable health crisis (Kerekes and Thornton, 1996). Such a risk assessment program may utilize the risk factors previously identified to target certain patients proactively. Nikolaus et al. (1995) were able to develop an instrument to assess nutritional risk in older persons. They argue that risk assessment is a major component of the medical management of older persons. Interventions are often designed based on the risk factors identified. For example,

an intervention program which targets older persons who are frail and who have chronic illness has demonstrated a significant decrease in emergency room visits, admissions, and length of stay in a risk assessment program in St. Joseph Medical Center (Swindle, Weyant and Mar, 1994).

Cargill (1992) developed criteria to help identify those patients at highest risk for problems related to medication noncompliance. These criteria included: multiple medications (more than three medications per day prescribed), medication regimen changes (a change in the past six months), multiple prescribers, and memory, sensory, and cognitive deficits (unable to verbalize name or purpose and frequency of medication, unable to read the label, unable to calculate how many 10mg pills in a 20mg dose, and unable to judge appropriately administration times for twice a day dosing regimens)(Cargill, 1992). Cargill (1992) reported that those older persons with more risk factors were older and had more medications prescribed, but they did not have different compliance patterns than those with fewer risk factors.

Identifying possible risk factors for drug-related morbidity based on theory has been a difficult problem. Strand et al. (1991) used the following approach to identify possible risk factors,

> we identify three categories of risk factors that can affect the type and level of pharmacotherapeutic risk: (1) risk factors associated with the patient's clinical characteristics, (2) risk factors associated with the patient's disease, and (3) risk factors associated with the patient's pharmacotherapy. The interaction of these three types of risk factors ultimately determines the level of risk associated with a patient's pharmacotherapy and therefore the level of pharmaceutical care required of the pharmacist. (Strand et al., 1991, p.549)

The approach used in this study will be different. Possible risk factors for PDRM in older adults will be identified by careful consideration of the high leverage points within the medication use system and the biopsychosocial model of disease etiology and therapy. Based on this conceptual basis and empirical evidence, possible risk factors for PDRM will be entered into logistic regression models for PDRM. Therefore, risk factors in this study will be those variables that help to explain some proportion of the variance of PDRM in older persons. Variables with odds

ratios greater than one will be positive risk factors for PDRM, while variables with odds ratios less than one will be negative risk factors for PDRM. This approach will also allow estimation of the proportion of variance in PDRM in older persons that can be accounted for by these risk factors.

Risk factors for PDRM may be used in a variety of ways. First, if health care professionals know that an individual has one or more risk factors for PDRM, a proactive change in the medical care of that patient may be made to help prevent the occurrence of PDRM in the future. This knowledge will hopefully allow health care professionals to anticipate the possibility of PDRM occurring in individual patients. Boult et al. (1998) argue that high-risk older persons should be identified so that a comprehensive assessment of their health-related needs may be performed, and interventions planned to meet these needs. In the medication use system, physicians, in particular, should consider these risk factors when creating a therapeutic plan for the patient. Risk factors may be considered as indicators that help direct the health care professional to patients with potential problems. Koecheler et al. (1989) used six prognostic indicators (or risk factors without the empirical evidence) for patients who might warrant pharmacist monitoring. Second, the risk factors identified can be related to the medication use system for interpretability in order to determine the best possible manner of use. For example, if a risk factor is known to relate to patient monitoring, then every attempt should be made to ensure that the patient receives proper monitoring. This is important because often risk factors can not be eliminated from the individual patient (e.g. gender), so proper management of the patient becomes paramount. Finally, risk factors may be used to help in the allocation of scarce healthcare resources.

Summary Of The Conceptual Models To Be Used In This Study

In summary, the conceptual framework that will be used for the study *risk assessment of preventable drug-related morbidity in older persons* is based on the application of systems theory in two models. The first model that incorporates systems theory is the medication use system. This model applies many of the central themes of systems theory, including the interdependency of related things, identification of recurring structures, feedback and communication loops, system goals, and identification of main change (or high leverage) points (Senge, 1994; Laszlo, 1973; Nadler and Hibino, 1994). In the medication use system itself, a structure has been proposed and essential elements identified, which includes key communication and feedback loops between the physician, patient, and pharmacist, a system goal of improving patient outcomes, and high leverage points such as patient monitoring (Hepler and Grainger-Rousseau, 1995; Hepler and Strand, 1990). The biopsychosocial model, also based on systems theory, permits a holistic evaluation of patients that includes cultural, social, psychological, and behavioral dimensions of illness. Risk factors for PDRM in older persons will be identified based on these first two models.

CHAPTER 3
REVIEW OF THE LITERATURE

The following review of the literature will focus on drug-related morbidity and mortality in older persons, identification of older persons at high risk of medical problems, and finally, a review of prediction models for drug use in older persons.

Drug-Related Morbidity and Mortality in Older Persons

Drug-related morbidity and mortality is a problem of special consideration in older persons. The incidence of drug-related morbidity seems to be higher in older persons, although it declines in the last decades of life (80 plus years) and age does not appear to be an independent risk factor for drug-related morbidity (Carbonin et al., 1991; Gurwitz and Avorn, 1991). Still, Campbell (1981) argues the increasing number of older persons and their prominent utilization of healthcare services, particularly medications, naturally extend itself to concern about the high risk drug-related morbidity and mortality in this population.

Fincham (1996) gives a succinct statement as to the extent of this problem in older persons:

> providing for consistent and appropriate use of drugs is exceedingly important for the ambulatory elderly. Studies have shown that when it does not occur, hospitalizations occur due to noncompliance and to the occurrence of avoidable adverse drug reactions. Significant predictors of preventable hospital readmission for the elderly include the occurrence of preventable adverse drug reactions, noncompliance, overdose, lack of a necessary drug therapy, and underdose. Others have noted that 50% of drug-induced illnesses that require hospitalization could have been avoided. Elsewhere, researchers have estimated that 75% of medications are misprescribed for the elderly, with overuse and underuse rampant. There must be increasing efforts to ensure continuity of care for the ambulatory elderly to avoid these and other drug-related problems. Because drug use

> in the elderly is dynamic and increases with proximity to death, pharmacists are key players to help the elderly avoid these drug-related problems. (Fincham, 1996, p.525)

The literature is rich with examples to substantiate these concerns. Grymonpre et al. (1988) determined that 19 percent of all hospital admissions (23 percent of all admissions that involved prescription drugs) of patients aged 50 and older exhibited at least one type of drug-related morbidity and mortality in a tertiary care hospital in Manitoba, Canada. The major types of drug-related morbidity and mortality identified were adverse drug reactions (48 percent), intentional noncompliance (27 percent), treatment failures (19 percent), alcohol-related problems (14 percent) and medication errors (10 percent) (Grymonpre et al., 1988).

Ostrom et al. (1985) studied medication use in 183 independently living seniors in Seattle and reported the prevalence of many medication problems. Seventy-five percent of the older persons had at least one potential medication problem, with a label discrepancy (37 percent), potential drug interaction (27 percent), underuse of medication (24 percent), inability to read label (14 percent), and failure to open prescription vial (12 percent) being the most common problems (Ostrom et al., 1985).

Some researchers have identified drugs that have a particularly high risk for drug-related morbidity and mortality in older persons. Dalziel, Byszewski and Ross (1996) constructed a list of the top ten problem drugs in the older persons (they failed to provide any empirical evidence as to why these certain medications made the list, however): Non-steroidal anti-inflammatory drugs (NSAIDS), benzodiazepines, amitriptyline, fluoxetine, anticholingerics/antihistamines, over-the-counter drugs/alcohol, cimetidine, centrally-acting antihypertensives/beta-blockers, digoxin, and irritant laxatives/colacel. The most commonly implicated drugs in 162 cases of drug-related morbidity and mortality identified in another study were: systemic steroids, digoxin, nonsteroidal anti-inflammatory agents, methyldopa, calcium channel blockers, beta-blockers, theophylline, furosemide, sympathomimetics, thiazides, and benzodiazepines (Grymonpre et al.,

1988). In a study of drug-related hospital admissions, hypoglycemic and diuretic agents were the two most implicated drugs (Nelson and Talbert, 1996).

Beers et al. (1991) used the Delphi technique to develop 30 factors defining inappropriate medication use in the nursing home setting. Using modified versions of these criteria, other authors determined that 14.0 to 23.5 percent of older adults living in the community were using at least one inappropriate drug (Stuck et al., 1994; Wilcox, Himmelstein and Woolhandler, 1994). Beers' criteria was limited by its failure to include specific reasons why these "inappropriate" drugs should be avoided, which newer lists have attempted to include (Buerger, 1998).

Several authors have studied specific types of PDRM in older persons, such as falls and hip fractures. Ray, Griffin and Downey (1989) studied a population of older persons in Saskatchewan, Canada, and determined that the risk relative risk of hip fracture was higher for users of long half-life benzodiazepines (1.7) as compared to those who used short half-life drugs (1.1). Prudham and Grimley-Evans (1981) concluded that older persons who reported falls in a one-year period were taking statistically significantly more tranquilizers and diuretics than older persons who did not report having at least one fall. A case-control study assessed the risk of hip fractures associated with four classes of psychotropic drugs and determined that there was an increased risk with concomitant use of long-half-life hypnotic-anxiolytics, tricyclic antidepressants, and antipsychotics (Ray et al., 1987).

Drug-related morbidity and mortality in older persons has been documented to occur in many different locations, such as the ambulatory, nursing home, emergency room, and inpatient settings. In a study conducted in the early 1960's in 178 older persons ambulatory patients with chronic illness, 59 percent were found to have at least one type of drug-related morbidity and mortality, with 26 percent of the cases viewed as being serious (Schwartz et al., 1962). Aronow (1996) looked at the use of digoxin in 500 consecutive nursing home admissions and concluded

that 47 percent of the patients had an inappropriate indication for use. In the nursing home setting, it has been estimated that the total cost of drug-related morbidity and mortality without the services of consultant pharmacists is $7.6 billion annually (Bootman, Harrison and Cox, 1997). Adams et al. (1987) found that a large percentage of older persons who had an emergency room visit at a hospital in England had a DRP in the categories of drug interaction and improper drug selection. Six percent of older persons had a serious drug-diagnosis or drug-laboratory contraindication and 19.7 percent of patients had a drug-drug interaction, although not all of these were deemed to be clinically significant (Adams et al., 1987). Ray, Federspeil and Schaffner's (1980) study of antipsychotic drug use in Tennessee nursing homes suggested that many older persons were using drugs without an indication. A study of the use of sedative-hypnotics in hospitalized older persons revealed that 20 percent of the prescriptions exceeded recognized dosing guidelines and this was associated with a greater severity of illness (Zisselman et al., 1996).

Identification of Patients at High Risk of Medical Problems in Older Persons

A risk factor is a variable statistically associated with an outcome event. Many researchers have attempted to identify specific risk factors for health care resource utilization or morbidity in older persons. These researchers reason that because health care resources are limited it may be best to find those patients who are at particular risk and concentrate on those individuals. For example, Nikolaus et al. (1995) identified risk factors associated with malnutrition in older persons. The main risk factors were a high number of prescription drugs, social isolation, chronic and painful diseases, and high consumption of alcohol or cigarettes (Nikolaus et al., 1995). Their study was limited to hospitalized older persons so the authors admit that further research must be done in other settings. Fowles et al. (1996) compared self-

reported health status (ShortForm-36) and diagnosis (Ambulatory Care Groups) to demographic information and found that the former two were much better predictors of health care expenditures in older adults. Therefore, it appears that demographic information is not sufficient to predict high utilizers of health care and other factors must be considered.

Kramer, Fox, and Morgenstern (1992) describe the approaches taken by seven health maintenance organizations (HMOs) with Medicare-risk contracts to identify high risk patients. One of these HMOs, Kaiser Permanente Southern California, identified approximately 35 percent of all inpatient admissions as being a high risk group through the use of the following criteria: age 80 or above, cerebral vascular accident, new fracture, admitted from a nursing home, a hospital readmission within ninety days that was unplanned, immobility, activities of daily living impairment, malnutrition, incontinence, confusion, prolonged bed rest, history of falls, depression, or existence of social problems (Kramer, Fox and Morgenstern, 1992). Kramer, Fox and Morgenstern (1992) did not state whether these initiatives to identify high risk patients were successful.

Stuck et al. (1994) studied patient factors associated with a risk of using an "inappropriate medication" in older persons by performing a multivariate logistic regression analysis. It was determined that a depression score was a risk factor, however, age, gender, income, number of chronic diseases, and activities of daily living score were not predictors (Stuck et al., 1994). Wilcox, Himmelstein, and Woolhandler (1994) also examined the risk of using an inappropriate medication in older persons and determined that patient risk factors were a high number of prescription medications, female gender, people living in the Southern United States, poor self-rated health status, and Medicaid beneficiaries.

Risk factors associated with drug-related morbidity have also been identified for older persons. Grymonpre et al. (1988) determined that the risk of a drug-related morbidity in patients aged 50 and older was related to the number of diseases and number of drugs used, but not to

age, health score, or gender. Hurwitz (1969) reported that predisposing risk factors associated with drug-related morbidity included an age of 60 or greater, female gender, previous adverse drug reaction, and history of allergic disease. In a review of the English-language literature, Gurwitz and Avorn (1991) found that age is not an independent risk factor for drug-related morbidity, but rather patient-specific and functional characteristics are more important. Therefore, it appears that the literature is rich in examples of possible risk factors for PDRM in older persons.

Prediction Models for Drug Use in Older Persons

There is some evidence in the literature that prediction models can be created to identify individuals who are at risk of DRPs and these models can facilitate the development of interventions. Beers et al. (1992) developed an operational definition of inappropriate medication use in older persons in the nursing home setting and subsequent studies were able to use this definition to determine the degree of inappropriate use and develop intervention strategies to help correct this problem. Koecheler et al. (1989) developed six prognostic indicators for patients who might warrant pharmacist monitoring: (1) five or more medications in present drug regimen, (2) 12 or more medication doses per day, (3) medication regimen changed four or more times during the past 12 months, (4) more than three concurrent disease states present, (5) history of noncompliance, and (6) presence of drugs that require therapeutic drug monitoring. Evidence of adverse outcomes related to drug therapy was identified in 33.1 percent of charts, based on the use of these indicators (Koecheler et al., 1989). McGhan, Wertheimer, and Rowland (1982) used Medicaid data to develop multivariate predictive equations to identify patients with drug therapy problems.

In a recent study, McElnay et al. (1997) developed a risk model for predicting drug-related morbidity and mortality in older persons, similar to the approach used in this study. Their model was able to predict drug-related mortality and morbidity in older persons with a

specificity of 69 percent, a sensitivity of 41 percent, and an overall accuracy of 63 percent (McElnay et al., 1997). McElnay et al. (1997) identified seven variables which influenced the risk of drug-related morbidity and mortality: digoxin, antidepressants, chronic obstructive airways disease, angina, abnormal potassium level, and patient belief that their medication was in some way responsible for their hospital admission (McElnay et al., 1997).

Wilcox, Himmelstein, and Woolhandler (1994) state that measuring preventable drug-related morbidity and mortality in the community setting is difficult but it is extremely important since only a small proportion of drug-related morbidity results in hospital admissions and many problems may be unreported or unrecognized. Therefore, there appears to be a continued need for better prediction models of drug-related morbidity and mortality in older persons. Also, the McElnay study did not consider preventability. Furthermore, there are no operational definitions of PDRM in the peer-reviewed medical literature. The development of such definitions would contribute to the conceptual framework of a systems approach to the medication use system.

Research Assumptions and Hypotheses

The research assumptions and hypotheses that will serve as the basis for this study are proposed within the context of systems theory applied to the medication use system, the biopsychosocial model of disease etiology and therapy, and the ability to use conditional probabilities to identify at-risk individuals. As described earlier, while PDRM has been previously determined to be an important problem within the medication use process, operational definitions have not been adequately developed and the method to best identify those individuals at-risk is unknown. Four research questions that address these unresolved problems will be investigated. Based on the literature reviewed earlier in this chapter, and the conceptual framework discussed in chapter two, propositions were made for all four of these research questions.

Research Assumptions

The first research question is directed at the creation of operational definitions of PDRM. A research assumption related to this research question was proposed. This research assumption had to be met before the other research questions could be investigated. This research assumption is as follows:

A1A: Valid operational definitions of PDRM can be developed by a panel of geriatric medicine experts.

This assumption proposes that operational definitions of PDRM, consisting of criteria for specific types of PDRMs in older persons, can be developed and tested for validity. Previous authors have succeeded in creating algorithms for the assessment of adverse drug reactions (one type of DRP that can lead to PDRM). These algorithms have been tested for validity (Karch and Lasagna, 1977; Hutchinson et al., 1979; Kramer et al., 1979; Leventhal et al., 1979; Naranjo et al., 1981). Schumock and Thornton (1992) have created criteria to determine the preventability of adverse drug reactions, which has been subsequently used by others (Pearson et al., 1994). As explained in the next chapter, an attempt will be made to demonstrate the validity of the operational definitions of PDRM, although the lack of an accepted "gold standard" for PDRM is a limitation.

The consensus method to be used is the Delphi technique. Therefore, research question one was refined to focus on the usefulness of developing operational definitions of PDRM with the Delphi technique. The utilization of expert panels via the Delphi technique to generate consensus on healthcare issues has been quite extensive (Roberts, Sek Khee and Philp, 1994; Butterworth and Bishop, 1995; Megel, Barna Elrod, and Rausch, 1996). This includes its use to determine criteria for medication use in older persons. Fouts et al. (1997) used the Delphi technique to identify risk factors for DRPs in older persons. Beers et al. (1991) used the Delphi technique with 13 experts to reach consensus on explicit criteria for determining inappropriate medication use in nursing home residents. Therefore, it seems there is sufficient evidence that

the use of an expert panel in the creation of operational definitions for PDRM in older persons is reasonable and not without precedent.

Research Hypotheses

The second research question deals with the identification of major risk factors for PDRM in older persons. The specific hypotheses proposed to address this research question are the following:

H1A: *Digoxin use* will be a risk factor for PDRM in older persons.

H1B: *Antidepressant drug use* will be a risk factor for PDRM in older persons.

H1C: *Long-acting benzodiazepine use* will be a risk factor for PDRM in older persons.

H1D: *Antihypertensive drug use* will be a risk factor for PDRM in older persons.

H1E: *Gastrointestinal disorders* will be a risk factor for PDRM in older persons.

H1F: *Lung conditions* (lung disease, emphysema, bronchitis and asthma) will be a risk factor for PDRM in older persons.

H1G: *Kidney disease* will be a risk factor for PDRM in older persons.

H1H: *A history of falling* will be a risk factor for PDRM in older persons.

H1I: *Four or more prescribers* will be a risk factor for PDRM in older persons.

H1J: *Six or more prescription medications* will be a risk factor for PDRM in older persons.

H1K: *Four or more recorded diagnoses* will be a risk factor for PDRM in older persons.

H1L: *A previous adverse drug reaction* will be a risk factor for PDRM in older persons.

H1M: *High alcohol consumption* will be a risk factor for PDRM in older persons.

H1N: *Self-assessment of poor health status* will be a risk factor for PDRM in older persons.

H1O: *Trouble paying for medications* will be a risk factor for PDRM in older persons.

H1P: *Difficulty taking medications* will be a risk factor for PDRM in older persons.

H1Q: *Patient belief that they are taking too many medications* will be a risk factor for PDRM in older persons.

H1R: *Female gender* will be a risk factor for PDRM in older persons.

This proposition is based on (1) reports of the risk factors associated with different kinds of drug-related problems and drug-related morbidity that are found in the peer-reviewed medical literature, and (2) identification of possible risk factors as they might relate to the medication use system and the biopsychosocial model of disease etiology and therapy. The rationale for each individual risk factor is as follows.

Several variables relate monitoring of drug therapy:

H1A: *Digoxin use*

There is considerable evidence in the medical literature that *digoxin use* is a risk factor for adverse drug reactions and drug-related morbidity and mortality. Williamson and Chopin (1980) determined that digoxin is one of the highest risk drugs for drug-related hospital readmissions in older persons. Digoxin was the most implicated drug in an inpatient study involving 193 adverse drug reactions, accounting for 21 percent of all adverse drug reactions (Ogilvie and Ruedy, 1967b). Digoxin has been labeled one of the top ten problem drugs in older persons (Dalziel, Byszewski and Ross, 1996), and it was also identified as a risk factor for drug-related morbidity in older persons (McElnay et al., 1997). A multidisciplinary panel of health professionals in long-term care listed it as a risk factor for drug-related problems in elderly nursing home residents (Fouts et al., 1997).

There are several reasons why *digoxin use* may be a risk factor for PDRM in older persons. It is a water-soluble drug and has a smaller volume of distribution in older persons, therefore, it requires a lower dose (Harper, Newton and Walsh, 1989). Digoxin is also implicated in many drug-interactions and elimination of the drug may be a problem in older persons since there is an age-related loss of renal function. Digoxin can also cause failure to thrive in older persons through a diminished appetite (Harper, Newton and Walsh, 1989). Finally, digoxin

toxicity manifestations are often subtle or atypical in older persons (Dalziel, Byszewski and Ross, 1996).

Many of these problems with *digoxin use* in older persons may also relate to inappropriate prescribing, lack of patient advice or poor patient monitoring. As discussed in chapter two, all these factors can impact PDRM. This is especially true in older persons, as inadequate patient education on prescribed drugs was a factor that increased the risk of drug-related morbidity in older persons (French, 1996).

H1B: *Antidepressant drug use*

There is also considerable evidence in the medical literature for including *antidepressant drug use* as a possible risk factor for PDRM in older persons. Certain antidepressants (amitriptyline and fluoxetine) were identified as being two of the top ten problem drugs in older persons (Dalziel, Byszewski and Ross, 1996), and McElnay et al. (1997) also determined that antidepressant use was a risk factor for drug-related morbidity in older persons.

Like digoxin, patient monitoring is extremely important for antidepressants in older persons. In particular, tricyclic antidepressants are highly bound and there are lower albumin levels in older persons so the free fraction is greater, increasing the likelihood of drug toxicity (Harper, Newton and Walsh, 1989). Tricyclic antidepressants have anticholingeric/ antihistaminic side effects that are more evident in older persons.

H1C: *Long-acting benzodiazepine use*

There is considerable evidence in the medical literature that *long-acting benzodiazepine use* is a risk factor for adverse drug reactions and drug-related morbidity and mortality. Williamson and Chopin (1980) determined that long-acting benzodiazepines are one of the highest risk drug classes for drug-related hospital readmissions in older persons, and they were identified as one of the top ten problem drugs in older persons (Dalziel, Byszewski and Ross, 1996). They were also a risk factor for adverse drug reactions associated with global cognitive impairment in older persons (Larson et al., 1987). A multidisciplinary panel of health

professionals in long-term care listed it as a risk factor for drug-related problems in elderly nursing home residents (Fouts et al., 1997).

There are many physiological reasons why *long-acting benzodiazepine use* may be a risk factor for PDRM in older persons. Long-acting benzodiazepines are fat-soluble and have a larger volume of distribution in older persons, leading to increased storage and prolonged half-life (Harper, Newton and Walsh, 1989). Also, older persons are more sensitive to the effects of benzodiazepines (Harper, Newton and Walsh, 1989). The oxidative metabolism of long-half life benzodiazepines is often impaired in older persons (Harper, Newton and Walsh, 1989). As a result, they can cause depression, falls, confusion and withdrawal symptoms. French (1996) argues that age-related physiological changes that alter drug kinetics and pharmacological responses to the prescribed medication are factors that increase the risk of drug-related morbidity in older persons. Therefore, for *long-acting benzodiazepine use*, it appears that dosing and drug monitoring are two critical elements needed to diminish PDRM in older persons.

H1D: *Antihypertensive drug use*

At least two studies have identified *antihypertensive drug use* as a possible risk factor for drug-related morbidity. This drug class was a risk factor for adverse drug reactions associated with global cognitive impairment in older persons in the Larson study (Larson et al., 1987), and it was one of the highest risk drugs for drug-related hospital readmissions in older persons in another study (Williamson and Chopin, 1980). Also, centrally-acting antihypertensives/ beta-blockers was identified as being one of the top ten problem drugs in older persons (Dalziel, Byszewski and Ross, 1996).

Antihypertensive drugs have been well documented to cause drug-related morbidity in older persons. Many antihypertensives have central nervous system side effects and may cause acute confusion, hallucinations, impairment of memory, and reduced ability to perform complex psychomotor tasks (Harper, Newton and Walsh, 1989). Older persons are also particularly susceptible to depression and postural hypotension from certain antihypertensives. Therefore, it

appears that monitoring is also an important element of care for older persons who are taking this class of drugs.

H1E: *Gastrointestinal disorders*

Gastrointestinal disorders was previously identified in one study has being a risk factor for drug-related morbidity in older persons (McElnay et al., 1997). This could be because medications used for gastrointestinal disorders are often used improperly (Tamblyn et al., 1997; Moride et al., 1997) and many of these medications have been associated with drug-related morbidity in older persons (Harper, Newton and Walsh, 1989; Dalziel, Byszewski and Ross, 1996). Therefore, it appears that elements three (appropriate prescribing for explicit objectives) and six (monitoring) of the eight necessities for safe and effective drug therapy may also be potential problem areas for patients with *gastrointestinal disorders*.

H1F: *Lung conditions* (emphysema, bronchitis or asthma)

Chronic obstructive airways disease was previously identified in one study has being a risk factor for drug-related morbidity in older persons (McElnay et al., 1997). Patients with lung diseases such as asthma are often on medications that require special monitoring and it has been argued that these diseases can not be adequately explained by the biomedical model. For example, severity of asthma symptoms may depend on such things as cleanliness of living conditions and activities of daily living, which are better explained by the biopsychosocial model. Therefore including *lung conditions* as a risk factor appears to be compatible with the biopsychosocial model of disease and with the importance of monitoring drug therapy.

H1G: *Kidney disease*

The presence of *kidney disease* will be included as a possible risk factor for PDRM based on both the medical literature and theoretical considerations. A multidisciplinary panel of health professionals in long-term care listed decreased kidney (renal) function as a risk factor for drug-related problems in elderly nursing home residents (Fouts et al., 1997). Renal failure was found to be an associated factor to drug-related morbidity in a retrospective study in Chile (Zilleruelo, Espinoza and Ruiz, 1987). Older persons may be at a special risk of this. Renal blood

flow and glomerular filtration rate decrease with age (Harper, Newton and Walsh, 1989). This leads to an elevated drug level and prolonged half-life for drugs excreted by the kidney. This can cause drugs to accumulate and toxicity to develop. Therefore, prescribing proper doses of many medications and drug level monitoring for PDRM are very important. As well, patient-specific differences in renal function are great in older persons, which the biopsychosocial model considers.

H1H: *A history of falling*

A history of falling was found to be a risk factor for drug-related morbidity associated with global cognitive impairment in older persons in one study (Larson et al., 1987). In contrast, *a history of falling* was not found to be a risk factor for drug-related morbidity in a later study (Carbonin et al., 1991).

A history of falling may be a risk factor for PDRM in older persons because many different drug classes, such as long-acting benzodiazepines, antihypertensives, and others have been documented to cause falls. Therefore, it seems that appropriate prescribing, patient advice, patient participation in care, monitoring, and appropriate documentation of previous falls may be key elements to help prevent PDRM in older persons.

Several variables relate to the importance of communication for optimal drug therapy:

H1I: *Four or more prescribers*

Four or more prescribers will be included as a possible risk factor, mainly based on theoretical considerations. French (1996) did document that several providers prescribing therapy independently was a factor that increased the risk of drug-related morbidity in older persons. Theoretically, if a patient has multiple prescribers, PDRM could develop from competing prescribing objectives, and poor documentation and communication of information and therapy decisions.

H1J: *Six or more prescription medications*

There is considerable evidence in the medical literature that the risk of drug-related morbidity increases with an increase in the number of medications in the drug regimen. As early

as 1969, Hurwitz observed that patients with drug reactions had significantly more drugs during their hospital stay then those who did not develop drug reactions. Five or more medications was found to be the primary risk factor in a study of potential drug-drug interactions (Braverman et al., 1996), and taking more than four drugs was found to be a risk factor of drug-related morbidity (Carbonin et al., 1991). A multidisciplinary panel of health professionals in long-term care said elderly nursing home patients who take nine or more medications are at risk for drug-related problems (Fouts et al., 1997). Larson et al. (1987) looked at the relationship between the number of medications and cognitive impairment and determined that the relative odds for adverse drug reactions related to cognitive impairment was 9.3 for patients taking four or five drugs, and 13.7 for patients taking six or more drugs. Finally, five or more drugs in a regimen was a prognostic indicator chosen to identify ambulatory patients who warranted special pharmacist monitoring (Koecheler et al., 1989).

It appears that as the number of medications in a regimen increases, the opportunity for inappropriate prescribing, dispensing/administration errors, inadequate patient advice, lack of patient participation in care, inadequate monitoring, and poor documentation and communication all increase.

H1K: *Four or more recorded diagnoses*

Patients with several diseases appear to be at greater risk for drug-related mortality. Carbonin et al. (1991) found that more than four active medical problems was a risk factor for drug-related morbidity. "Patients having more than three diseases" was used as a prognostic indicator chosen to identify ambulatory patients who warranted special pharmacist monitoring (Koecheler et al., 1989). A multidisciplinary panel of health professionals in long-term care listed "more than six active chronic medical diagnoses" as a risk factor for drug-related problems in elderly nursing home residents (Fouts et al., 1997).

The biopsychosocial model may be important in understanding why patients with several diseases may be at an increased risk of PDRM. Gurwitz and Avorn (1991), upon reviewing the medical literature on drug-related morbidity, stated that patient-specific physiologic and

functional characteristics are important in predicting drug-related morbidity. The biopsychosocial model allows for consideration of the patient-specific differences. As well, timely recognition of signs and symptoms and appropriate documentation may be even more important for patients with several concurrent diseases. Patients with several diseases are often in the care of a general practitioner and one or more specialists, who may not always communicate their therapeutic plans, and which may be in conflict.

H1L: *A previous adverse drug reaction* (ADR)

It appears that patients who had a previous adverse drug reaction are at increased risk for experiencing another event in the future. *A previous adverse drug reaction* was previously found to be a predisposing factor in adverse reactions to drugs (Hurwitz, 1969). *A previous adverse drug reaction* was found to be an associated factor with adverse drug reactions in a retrospective study in Chile (Zilleruelo, Espinoza and Ruiz, 1987). A multidisciplinary panel of health professionals in long-term care listed it as a risk factor for drug-related problems in elderly nursing home residents (Fouts et al., 1997). Also, in one study involving 177 patients who had suffered adverse reactions during hospitalization, 32 percent had a second reaction (Ogilvie and Ruedy, 1967a).

There are several reasons why these individuals may be at particular risk of PDRM. They may have physicians, prescribers or patient-specific factors that contribute to poor prescribing, dispensing, administration, patient advice, patient participation in care, monitoring or documentation. As well, the biopsychosocial model may be useful to help explain why specific patients are at risk of experiencing a second drug-related morbidity. The most important factor, however, may be poor documentation and communication of their previous adverse drug reaction.

Several variables relate to the biopsychosocial model and patient-specific differences:

H1M: *High Alcohol Consumption*

There is some evidence in the medical literature that *high alcohol consumption* is associated with drug-related morbidity. Alcohol consumption was found to be a risk factor of

drug-related morbidity (Carbonin et al., 1991) and alcohol was listed as one of the top ten problem drugs in older persons (Dalziel, Byszewski and Ross, 1996). The side effects of alcohol intake in older persons are potentiated because both metabolism and excretion of alcohol are altered with aging. In older persons, recognition of alcoholism is often difficult and delayed because the manifestations may be subtle or erroneously attributable to normal aging (Dalziel, Byszewski and Ross, 1996). Alcohol, when combined with many medications, can be dangerous and lead to such events as falls. When a patient consumes alcohol and is taking medications, patient advice and monitoring are both critical elements. As well, *high alcohol consumption* is associated with sociological, behavioral, and psychological factors that can be best explained by the psychosocial model of disease.

H1N: *Self-assessment of poor health status*

Self-assessment of poor health status will be included as a possible risk factor, also primarily based on theoretical considerations. There is some evidence in the literature that self-assessment of health as poor is associated with mortality (Fried, Pollack and Tinetti, 1998). In addition, patient-specific physiologic and functional characteristics are important in predicting drug-related morbidity (Gurwitz and Avorn, 1991). The biopsychosocial model is important in helping to explain this as a possible risk factor for PDRM. This model allows the inclusion of psychological and behavioral elements in illness.

H1O: *Trouble paying for medications*

Trouble paying for medications will be included as a possible risk factor for PDRM based on theoretical considerations. A patient who reports that they are having trouble paying for medications may exhibit poor medication compliance with their medication regimen due to the cost of the medications. The expense of the drug is a factor that contributes to poor compliance. Schneider et al. (1991) showed that noncompliance is related to a belief that taking medications will not result in a successful medical outcome. Thus, *trouble paying for medications* may also relate to a reluctance to take medications because of a belief that they will not help to improve the health of the patient. O'Neil and Poirer (1998) showed that patients with poor perceptions of

their drug regimen had more adverse drug therapy outcomes. One study did determine that older persons who do not comply with prescribed medicines are at an increased risk of drug-related morbidity (French, 1996). Again, the biopsychosocial model is important in order to consider sociological variables in this model. As well, patient participation in care is important to prevent PDRM, and this includes compliance with medications and attributing medications with an improved health status.

H1P: *Difficulty taking medications*

Difficulty taking medications will be included as a possible risk factor for PDRM based on theoretical considerations. A patient's self-report that they are having difficulty taking medications may also relate to their attitude of taking medication. Grembowski et al. (1993) discovered that older persons with a low self-efficacy in health behaviors had poorer health. Therefore, it is conceivable that many older persons have low self-efficacy in taking medications and thus develop PDRM. The biopsychosocial model is important in order to consider behavioral variables in this model. As with the previous variable, patient participation in care is important to prevent PDRM, and this includes self-efficacy with taking medications. In addition, French (1996) claims that many older persons experience motor-sensory declines that contribute to an inability to properly take medications.

H1Q: *Patient belief that they are taking too many medications*

Patient belief that they are taking too many medicines will be included as a possible risk factor for PDRM based on theoretical considerations. This variable may also relate to the patient's attitude towards medications. Disagreement with the prescribed medication regimen is a factor that contributes to poor compliance. Highly complex medication regimens are associated with noncompliance (Haynes, Taylor, and Sackett, 1979). Also, patients who believe they are on too many medications may have low self-efficacy for taking medications, which may also lead to poorer health and PDRM. Again, the biopsychosocial model is important in order to consider behavioral variables in this model. As well, patient participation in care is important to prevent PDRM, and this includes compliance with medications.

One variable has been included based on empiric evidence, but it does not seem to directly relate to the conceptual models used in this study:

H1R: *Female gender*

Female gender has been identified as being a risk factor for drug-related morbidity in several studies. Hurwitz (1969) noted that females had significantly more drug-related morbidities than males. *Female gender* was found to be an associated factor with adverse drug reactions in a retrospective study in Chile (Zilleruelo, Espinoza and Ruiz, 1987). The odds ratio associated with having an ADR in older females as compared to males was found to be 1.9, although it was not statistically significant (Hallas et al., 1991). Finally, gender was found to be a determinant of both the frequency and characteristics of ADRs in a prospective drug surveillance study involving 1920 patients in Chile (Domecq et al., 1980). In contrast, *female gender* was not found to be a risk factor for ADRs in one study, although the odds ratio for an ADR was 1.22 (0.987-1.54, 95 percent confidence interval) (Carbonin et al., 1991). Zadoroznyj and Svarstad (1990) argue that by excluding female-specific drugs and conditions (e.g.; pregnancy) there is basically no difference in drug use between males and females.

The reason why *female gender* may be a risk factor for PDRM does not seem to be easily explained by any of the models used in this study but will be included for empirical reasons.

The third research question addresses whether there are general risk factors for PDRM and risk factors which might be drug or disease specific for PDRM. This research question is obviously closely related to the previous research question. The hypothesis proposed for this question is as follows:

H2: There will be both general risk factors for PDRM and risk factors that are drug or disease specific for PDRM

This proposition is based on the reports of the wide variation of risk factors associated with different kinds of PDRMs that are found in the peer-reviewed medical literature. As the

previous review of the literature showed, there seems to be some general risk factors for PDRM (poor health status, multiple prescribers, multiple disease states), and some drug-specific (digoxin, antihypertensives, etc.) and disease-specific (lung disease, kidney disease, etc.) risk factors for PDRM.

The fourth research question is whether the utilization of health care resources differs between patients with, and without, PDRM. The specific proposition hypothesized for this research question is the following:

H3: Older persons that have PDRM will consume more health care resources than those who do not have PDRM

This hypothesis suggests that there will be a significant difference in the health care resource utilization patterns between those older persons who do, and do not, have PDRM. Based on the literature previously reviewed, there is empirical support that those older persons who experience PDRM do consume more health care resources. Zisselman et al. (1996) concluded that those older persons who received sedative-hypnotics with doses exceeding the Health Care Financing Administration (HCFA) guidelines had increased hospital costs and longer lengths of stay as compared to those who did not receive these drugs or whose dosages did not exceed the guidelines (although the direction of causality is unknown). The very nature of PDRM often involves the consumption of valuable resources. For example, Bates et al. (1997) determined that those patients with a preventable adverse drug event (ADE) had an average increase of 4.6 days in length of stay and $5857 in total cost, and the annual costs attributable to all preventable ADEs was estimated to be $2.8 million for a 700-bed teaching hospital. Thus, based on this evidence, the proposition will be made that those who experience PDRM will have a higher utilization of healthcare resources.

CHAPTER 4
METHODS

The intent of this study was to (i) determine the issues in developing and using operational definitions of PDRM, (ii) identify major risk factors for PDRM in older persons, (iii) examine whether there are general risk factors for PDRM in older persons and drug, or disease, specific risk factors, and (iv) determine what is the relationship between PDRM and the utilization of healthcare resources.

To meet these objectives, this study was conducted in two phases. The first phase of the study concentrated on the dependent variable in this study: preventable drug-related morbidity (PDRM). In this phase, operational definitions of PDRM were created through the use of a geriatric medicine expert panel and validated using a chart abstract reviewer panel. The second phase of the study focused on the independent variables: hypothesized risk factors for PDRM. In this phase, the risk factors related to PDRM in older persons were identified using the study database: claims and quality of life data from the Florida Hospital Healthcare System Premier Care Plan Medicare population. This second phase of the study also involved the creation of a risk stratification system for PDRM and exploration into the relationship of PDRM and healthcare resource utilization.

Phase I: Operational Definitions of PDRM

The first research question described above was investigated in Phase I of the study. Phase I of the study involved the creation of operational definitions of PDRM in older persons. This was accomplished by a review of the medical literature, and the administration of a survey to a consensus panel of geriatric medicine experts. The validity of these definitions of PDRM

was explored through the use of a second panel: a chart abstract reviewer panel. These steps of the Phase I methodology are displayed in Table 4.1.

Operationalization of the Study Construct PDRM

In order to have the geriatric medicine expert panel agree on what is a PDRM, and for the purpose of the conceptual framework of this study, it was necessary to operationalize the term PDRM. A PDRM can be defined as an unwanted consequence of the medication use process that, with appropriate systems, adequately trained personnel and patients or caregivers, could have detected, predicted, controlled and avoided (Hepler and Strand, 1990). PDRM results from (a) unacceptable quality of care (e.g., failure to meet consensus guidelines) or (b) occurs after a *drug-related problem (DRP)*. A review of the literature of PDRM in older persons was presented in chapter 3 and its relationship to the medication use system and biopsychosocial model was explored in chapter 2.

An extension of this conceptual definition is that PDRM has four defining characteristics. The *DRP* that lead to the PDRM must be recognizable and the likelihood of a drug-related morbidity must be foreseeable. In addition, the cause(s) of the DRP (and subsequent drug-related morbidity) must be identifiable, and those causes must be controllable. *Preventable drug-related morbidity*, therefore, results from unrecognized or otherwise unresolved *DRPs*.

An operational definition of each of these four defining characteristics is as follows:

1. Recognizable. In order for a drug-related morbidity to be recognizable, the DRP that produced the drug-related morbidity must be observable (Hepler and Strand, 1990). This was determined by listing specific outcomes (morbidities) and patterns of care. A geriatric medicine expert panel was then asked to judge whether for most older persons, if health

Table 4.1 Phase I Methodology

Steps of the Phase I Methodology
Review of literature on PDRM, relationship to conceptual framework explored, and defining characteristics of PDRM studied
Review of literature to identify specific operational definitions of PDRM in older persons
Construction of survey for the Geriatric Medicine Expert Panel, in order obtain consensus on specific operational definitions of PDRM
Content review of survey by 8 individuals
Pilot test of survey mailed to 40 pharmacists
Revision of survey based on comments/responses from 28 respondents
Selection of Geriatric Medicine Expert Panel members
Administration of survey to Geriatric Medicine Expert Panel –Round 1 of Delphi
Administration of survey to Geriatric Medicine Expert Panel –Round 2 of Delphi
Consensus-approved operational definitions of PDRM obtained from the Geriatric Medicine Expert Panel
Identification of consensus-approved operational definitions of PDRM in study population
Abstracted chart reviews of a sample of patients with and without PDRM in study population
Administration of chart reviews to Chart Abstract Reviewer Panel to test for validity

professionals (physicians, pharmacists, etc.) should be able to **recognize** significant problems in this pattern of care.

2. Foreseeable. In order for a drug-related morbidity to be foreseeable, a reasonably prudent clinician would have recognized that the drug-related morbidity might follow if the recognized DRP were not resolved. This was determined by listing specific outcomes (morbidities) and patterns of care. A geriatric medicine expert panel was then asked to judge whether for most older persons, if health professionals should be able to **foresee the possibility of the outcome,** given those problems were not resolved.

3. Causality must be identifiable. Formal attribution algorithms, such as the Naranjo algorithm, DRAPE algorithm, and the Kramer algorithm, have been used in the past to identify causality for adverse drug events. Identification of causality for the drug-related morbidity was determined by listing specific outcomes (morbidities) and patterns of care. Causality typically involves seeing what to change. A geriatric medicine expert panel was then asked to judge whether most health professionals should **see how to change** the pattern of care to prevent the outcome.

4. Controllable. In order for the cause of a drug-related morbidity to be controllable, the clinician, patient, or caregiver must have been able to exercise restraint or direction over the presumed cause of the drug-related morbidity. In order to determine whether the cause of the drug-related morbidity was controllable, specific outcomes (morbidities) and patterns of care were listed. A geriatric medicine expert panel was then asked to judge whether most health professionals should **actually change** the pattern of care.

A drug-related morbidity was judged to be preventable only if the criteria for all four defining characteristics were met.

In this study, the standard of care used by the health care professional to assess these four definitions in specific clinical scenarios was not explicitly stated. It is therefore assumed

that the health care professionals used an implicit standard of care, such as their typical daily practice or clinical practice guidelines. This approach has the advantage of letting the health care professionals use their own professional judgement and years of clinical experience to determine whether a specific clinical scenario is a case of PDRM.

Review of Literature to Identify Specific Operational Definitions of PDRM in Older Persons

As previously discussed in Chapter 3, the literature contains a comprehensive account of the most commonly occurring drug-related morbidities in older persons. Many of these morbidities have been hypothesized to be preventable. The literature on drug-related morbidity since 1967 was reviewed for possible types of preventable drug-related morbidity. The search was limited to those morbidities that occur in older persons. Peer-reviewed medical articles and referenced texts were included in the literature review.

Based on the literature review, a list of 50 clinical scenarios (representing possible PDRMs occurring in older persons) was compiled. These clinical scenarios had to meet the following inclusion criteria: (1) well-referenced, (2) occur fairly commonly in the geriatric population, (3) result in serious adverse outcomes, and (4) searchable in the study database. Clinical scenarios involving specific laboratory values or drug dosages were excluded as this information was not available in the study database.

Survey Development

A survey instrument was constructed in order to evaluate whether these 50 clinical scenarios met the four defining characteristics of a PDRM. All clinical scenarios were listed in a similar format to facilitate reading. In this format, the outcome (morbidity) was listed first, with the pattern of care which lead to the outcome, listed second.

Expert review and pilot testing were used to assess the content validity of the survey. The survey, instructions for use, and cover letter were reviewed by eight experts in health

services research from the Department of Pharmacy Health Care Administration at the University of Florida for ease of use and to determine the relevance of the questions to existing conceptual frameworks. Based on their feedback, slight modifications were made.

A convenience sample of community, hospital, managed care, consultant, and academic clinical pharmacists from geographically diverse parts of the United States and Canada was selected for the pilot test. Before receiving the survey, all individuals were contacted by e-mail, fax or telephone to inform them to expect the survey. The list of 50 clinical scenarios was split in half and each half was given to 20 content reviewers, along with a cover letter and instructions for use. A total of 28 content reviewers completed the survey (15 completed the first half, 13 completed the second half), made comments, and returned the survey in time for analysis, for a 70 percent response rate.

Based on their feedback, slight modifications were made to the survey instrument. As well, based on the pilot test results, some clinical scenarios were dropped from the survey, and several new clinical scenarios were added to the survey instrument, leaving a total of 48 clinical scenarios.

Geriatric Medicine Expert Panel

In order to reach consensus on which clinical scenarios listed in the survey instrument were actual PDRMs, the Delphi technique was used. As Goodman (1987) explains:

> The Delphi technique is a survey method of research which aims to structure group opinion and discussion. It was first developed in the 1950s by the Rand Corporation in California as an attempt to eliminate interpersonal interactions as the controlling variables in decision making, as usually happens when groups of experts interact in meetings. Its purpose is to generate discussion and enable a judgement on a specified topic to be made so that policy decisions can be taken which can claim to represent a given group's wants and views (Goodman, 1987, pp.729).

Beers et al. (1991) argue that consensus methods, such as the Delphi technique, are useful because: (1) differences in published opinion may be overcome, (2) they can help create criteria

that address narrow clinical scenarios, and (3) they can incorporate supplemental information, such as physiological changes in older persons.

Duffield (1993) argues that the choice of panel members is critical in order for the Delphi technique to work correctly. Participants should be chosen based on their willingness to participate and their expert knowledge base (Goodman, 1987). With this in mind, a panel of seven members was chosen by the Chief Medical Officer of the Florida Hospital Healthcare System, with input from the principal investigator and the Director of Ambulatory Pharmacy at the Florida Hospital. This panel consisted of physicians with recognized credentials in geriatric medicine, physician administrators, and a geriatric specialty clinical pharmacist at the Florida Hospital. These individuals were all thought to be opinion leaders within the Florida Hospital Healthcare System and have extensive expertise in geriatric medicine. The Geriatric Medicine Expert Panel members are listed in Appendix A.

The principal investigator explained the survey in depth to each panel member before they completed the survey. This is because commitment and understanding of the Delphi technique at the start of the technique influences the time and consideration given to the technique by the participants (Goodman, 1987). Appendix B contains the cover letter, instructions for use and survey instrument for the panel members. As Appendix B shows, the panel members were asked to judge whether each of the 48 clinical scenarios met the four defining characteristics of a PDRM. One clinical scenario was listed twice in the survey to serve as a validity check, so there were actually 47 unique clinical scenarios. In addition, there was an open-ended question at the end of the survey, where panel members could suggest any additional operational definitions of PDRMs. Prior to the commencement of the Delphi rounds, the inclusion of operational definitions of PDRM was set as those that were chosen by a majority of panel members (at least four out of seven members). All seven panel members completed and returned the survey.

The round two survey was sent to the same seven panel members the following month. This survey contained the clinical scenarios that had survived round one and several new clinical scenarios that were suggested by the panel members. For each clinical scenario, the panel members were given their response (yes/no) from the previous round, the total group response, and all the comments made by the panel members. By providing comments from the previous round, consensus is reached quicker, usually in two rounds (Duffield, 1993). Round three consisted of the results from round two and a letter thanking each expert panel member.

Identification of Consensus-Approved Operational Definitions of PDRM in Database

The consensus-approved operational definitions of PDRMs were identified by first examining the study database for the outcomes related to the specific operational definitions of PDRM. This was performed by searching for the diagnosis codes related to these outcomes. Then, once the outcomes (morbidities) were identified, each patient case was individually searched to determine whether the associated pattern of care that led to the outcome was provided or not. If both the outcome and pattern of care matched the specific operational definition of the PDRM, then it was judged to have been a case of PDRM.

Validation of Operational Definitions of Preventable Drug-Related Morbidity

A chart abstract reviewer panel of five clinical pharmacists was used to further validate the Geriatric Medicine Expert Panel consensus-approved operational definitions of PDRM.

The first step was to choose the specific operational definitions of PDRM which occurred often enough in the study database to allow adequate determination of sensitivity and specificity (confidence intervals that did not include zero). The size was chosen to allow determination of a sensitivity and specificity of 67 percent. This would be better than the

sensitivity (41 percent) and near the specificity (69 percent) of an existing model to detect total adverse drug events in older adults (McElnay et al., 1997). It would also be comparable to models developed to predict adverse drug reactions related to digoxin (sensitivity 92.9 percent, specificity 61.8 percent) and theophylline (sensitivity 95.8 percent, specificity 84.0 percent) (Tschepik et al., 1990). Based on this target sensitivity and specificity, only two specific operational definitions of PDRM occurred often enough to be tested for validity: (1) patients with secondary myocardial infarction who did not receive ASA and/or a beta-blocker, and (2) patients with an emergency room visit and/or hospitalization due to hyperglycemia who were on an oral hypogylcemic and did not have regular hemoglobin A1c monitoring.

Second, abstracted chart reviews of these patients were performed. These chart abstracts were performed by a primary care pharmacy resident at the Florida Hospital. The instructions for the chart abstracts, the patient chart abstract review form, and samples are shown in Appendix C. The chart abstracts were all performed in the same format to allow for ease of reading by the Chart Abstract Reviewer Panel members. The chart abstracter was given the patient medical record numbers for all the patients who had the outcome regardless of whether they had the pattern of care related to that defined preventability. The chart abstracter was blinded as to whether the patient he was reviewing did, or did not, have a case of PDRM, as defined by the specific operational definition. All chart abstracts were done from the inpatient charts at the Florida Hospital and the outpatient laboratory computer system at the Florida Hospital. Chart abstracts could not be completed for 4 patients with the secondary myocardial infarction outcome and 1 patient with the hypergylcemia outcome because the medical charts could not be located. In all, 35 chart abstracts were performed for patients with secondary myocardial infarction and 31 patients with hypergylcemia.

All of the chart abstracts (n=66) were then given to the Chart Abstract Reviewer Panel, consisting of five pharmacists at the Florida Hospital. The pharmacists were chosen by the

Clinical Coordinator of Pharmacy at the Florida Hospital based on their availability, willingness to participate and experience working with the study population. Appendix D shows the background of the panel members. The principal investigator and chart abstracter met with the panel members to explain the instructions for use (see Appendix E), and to answer any questions the panel members might have. These pharmacists were given the two relevant consensus-approved operational definitions of PDRM and were asked to use them in determining whether the patients in the chart abstracts actually experienced a PDRM. If four or more of the five panel members judged a chart abstract to be a case of PDRM, then it was categorized as a PDRM. If three or fewer panel members judged a chart abstract not to be a case of PDRM, then it was categorized as not being a case of PDRM. The Fleiss measure of overall agreement was used to calculate the degree of agreement among the five raters (pharmacists) for classifying each patient (Fleiss, 1971). Others have advocated using this statistic in situations such as this, when there are more than two raters (Conger, 1980; Abedi, 1996).

From the results of the Chart Abstract Reviewer Panel, the sensitivity and specificity of these two specific operational definitions of PDRM was calculated. Sensitivity was calculated as the percentage of true PDRMs (defined as a PDRM by four or more of the panel members) that the operational definitions of PDRM labeled as such. Specificity was calculated as the percentage of abstracted chart reviews that were judged by the Chart Abstract Reviewer Panel not to be a PDRM, and the operational definition of PDRM labeled as not being a PDRM. A two-by-two table of true PDRMs and predicted PDRMs was constructed, based on the sensitivity and specificity.

It should be noted that for most screening tests or instruments, the sensitivity and specificity of that test is calculated by comparing the outcome of the test to a "gold standard". In this case there is no generally accepted "gold standard" for PDRM. However, if chart review by experts is considered to be such a standard, then the panel of five clinical pharmacists is being

used as the "gold standard", acknowledging certain limitations with this approach (see limitations section in chapter 6). The use of chart reviews by experts is commonly used as a "gold standard" in many other areas of healthcare, such as peer review organizations (PROs). In such cases, as in this study, the professional judgement of medical experts reviewing patient charts is used as the "gold standard".

Phase II: Identification of Risk Factors for PDRM

The methodology for the independent variables will now be discussed. The final three research questions described at the beginning of this chapter were investigated in Phase II of the study. Phase II of the study involved the identification of risk factors for PDRM. This was accomplished by reviewing the medical literature, identifying possible risk factors, and relating them to the conceptual framework and models used in this study. A database, consisting of enrollees from the Florida Hospital Healthcare System Premier Care Plan, was constructed to allow for the measurement of these risk factors. Next, a series of statistical analyses were performed to identify the risk factors. Finally, the relationship between PDRM and healthcare resource utilization was explored. These steps of the Phase II methodology are outlined in Table 4.2.

Selection of Possible Risk Factors for PDRM

As previously discussed in Chapters 1 and 3, the literature contains a rich account of risk factors for the most commonly occurring drug-related morbidities in older persons. The literature

Table 4.2 Phase II Methodology

Steps of Phase II Methodology
Review of literature on risk factors for PDRM and the relationship to conceptual framework and models explored
Hypotheses generated related to specific risk factors for PDRM in older persons, and semantic hierarchy developed
Study population identified
Construction of study database in order to identify and measure these hypothesized risk factors for PDRM
Logistic regression model of all 18 hypothesized risk factors for PDRM
Factor analysis of all 18 hypothesized risk factors for PDRM
Additional logistic regression models to identify other risk factors for PDRM
Risk stratification system developed
Relationship of PDRM and healthcare resource utilization explored

on drug-related morbidity since 1967 was reviewed for possible risk factors for PDRM. Peer-reviewed medical articles and referenced texts were included in the literature review.

Semantic Hierarchy of Risk Factors for Preventable Drug-Related Morbidity

Next, the relationship of these possible risk factors to the models (pharmaceutical care and biopsychosocial) discussed in chapter 2 was explored. Other possible variables were also identified, based on these models. Out of this process, 18 possible risk factors for PDRM were selected.

Based on this, a semantic hierarchy of risk factors for PDRM was developed and hypotheses related to the 18 risk factors were stated (chapter 3). A semantic hierarchy, as seen in Table 4.3, relates constructs to variables, and variables to measurements. Several possible risk factors relate to monitoring, as described by the medication use system: *digoxin use*, *antidepressant drug use*, *long-acting benzodiazepine use*, *antihypertensive drug use*, *gastrointestinal disorders*, *lung conditions*, *kidney disease*, and *a history of falling*. Several possible risk factors relate to patient-provider communication, as described by the medication use system: *four or more prescribers*, *a previous adverse drug reaction*, *six or more prescription medications*, and *four or more recorded diagnoses*.

Several possible risk factors relate to patient-specific aspects of drug use, as described by the biopsychosocial model: *difficulty taking medications*, *high alcohol consumption*, *self-assessment of poor health status*, *trouble paying for medications*, and *patient belief that they are taking too many medications*. *Female gender* did not seem to correspond to the conceptual framework but was included for empirical reasons. Several risk factors also seem to fit more than one construct: for example, *six or more prescription medications* may also be related to poor

Table 4.3 Semantic Hierarchy in Risk Factors for Preventable Drug-Related Morbidity

Constructs/ Concepts	**Preventable drug-related morbidity can be predicted by certain risk factors.** These risk factors relate to the key concepts of the medication use system and biopsychosocial model Monitoring	Communication	Patient Specific aspects
Variables	*Digoxin use* *Antidepressant drug use* *Long-acting benzodiazepine use* *Antihypertensive drug use* *Gastrointestinal disorders* *Lung conditions* *Kidney disease* *A history of falling*	*Four or more prescribers* *A previous adverse drug reaction* *Six or more prescription medications* *Four or more recorded diagnoses*	*Difficulty taking medications* *High alcohol consumption* *Self-assessment of poor health status* *Trouble paying for medications* *Patient belief that they are taking too many medications*
Measurements (observables) Examples	*Digoxin use*: FHHS and PCS claims data Dichotomous: 1=yes, no=0	*Four or more prescribers*: PCS claims data Dichotomous:1=4 or more prescribers, 0=3 or less	*Difficulty taking medications*: Personal Wellness Profile, "How difficult is taking medications for you?" *Dichotomous: 1= difficult ...very difficult/ can't do it, 0=not difficult*

monitoring as well as communication. A more comprehensive discussion of each risk factor is contained in chapter 3.

Study Population

In order to measure these risk factors, a study population was selected. The study population was drawn out of the larger pool of enrollees in the Florida Hospital Healthcare System Premier Care Health Plan. This was a health plan offered by the Florida Hospital Healthcare System, a provider-sponsored network with a Medicare contract. It was available to all Medicare beneficiaries who live in Orange, Osceola, and Seminole Counties of Florida and who were also enrolled in Medicare Part B. By U.S. federal law, however, those individuals who elected to receive the Medicare hospice benefit and those who had end-stage renal disease were not eligible for enrollment. Only those enrollees who completed the Personal Wellness Profile (PWP) Senior Assessment were included in the study. Enrollment into the Premier Care Health Plan began in January 1997, with approximately 7,000 enrollees by December 1997 and approximately 50 percent of these individuals completing the PWP. This comparable with the completion of health risk assessment tools in other Medicare programs (Kerekes and Thornton, 1996). Individuals who were enrolled in the plan anytime during 1997 were included in the study population.

Data Collection and Formation of the Study Database

The data used in this study consisted of (1) claims which were already collected as a natural part of the administration of the Premier Care Health Plan and (2) the Personal Wellness Profile Senior Assessment instrument which was completed by the enrollees. All claims

processed and surveys completed between January 1 and December 31, 1997 were included in the study.

More specifically, the study database consisted of three parts:

(1). Florida Hospital Healthcare System claims data. This data included all claims made in the outpatient and inpatient settings for this population, except for prescriptions filled in the ambulatory setting.

(2). PCS Outpatient Prescription Claims. This data includes all prescriptions filled for the plan enrollees in the ambulatory setting.

(3). Personal Wellness Profile (PWP) Senior Assessment. The PWP is an instrument that was given to all Premier Care plan members to complete (see Appendix F for the entire questionnaire). It is an instrument used to identify enrollees at high risk for health-related problems. It has been previously used by other health plans and its predictive validity has been verified and studied by Boult et al. (1994), Pacala, Boult, and Boult (1995), and Pacala et al. (1997). The PWP contains valuable information related to physical and functional status, which previous authors have shown to be related to utilization of health care services by older persons (Branch et al., 1981).

A central database containing these three data sets was constructed by a medical artificial intelligence company in Orlando, FL called MEDai. This database was completed on April 15, 1998 with approximately 95 percent of claims from 1997 processed at this time. A unique patient identifier was used to link these three data sets. All patient names were masked to protect patient confidentiality. The data set was provided to the principal investigator who discarded irrelevant data fields. Many variables were dichotomized for the purpose of the study. Considerable data manipulation was required for three of the study variables. While the study database as prepared by MEDai did contain a listing of all prescription drugs the patients had received, the drugs had to be organized into therapeutic classes for three of the study variables

(*long-acting benzodiazepine use*, *antidepressant drug use*, and *antihypertensive drug use*) for ease of use. For these three variables, an on-line database called Lexicon® was used to group all these drugs by national drug code (NDC) number to the appropriate therapeutic class (Multum Information Services, 1998). The accuracy of the Multum classification system was assessed for one drug in each of these three therapeutic classes (triazolam, luvoxamine, and diltiazem). All the patients in the study database who received these drugs were identified and it was determined whether the drug was placed into a therapeutic class, and if so, whether it was the correct class. Table 4.4 contains all 18 hypothesized risk factors and shows how they will be measured in this database. Table 4.5 contains the additional demographic variables to be considered for inclusion into the regression models, based on the bivariate analysis.

Statistical Analysis

Logistic Regression Model with the 18 Hypothesized Risk Factors

Initial data analysis was performed using a forward inclusion logistic regression procedure to determine which of the 18 hypothesized risk factors were significantly associated with PDRM. Larson et al. (1987) previously used this technique to determine which variables were associated with global cognitive impairment adverse drug reactions in older persons. McElnay et al. (1997) also used this technique to determine which variables were risk factors associated with drug-related morbidity in older persons in the inpatient setting. SAS® (SAS Institute Inc., 1993) and JMP IN® (Sall and Lehman, 1996) were used to create the regression models.

Table 4.4 Hypothesized Risk Factors and Their Measurement

Hypothesized Risk Factor	Measurement
Variables related to monitoring	
Digoxin use	Dichotomous: 1=yes, 0=no Measured from PWP drug question 1.
Antidepressant drug use	Dichotomous: 1=yes, 0=no Measured from PCS claims data.
Long-acting benzodiazepine use	Dichotomous: 1=yes, 0=no Measured from PCS claims data.
Antihypertensive drug use	Dichotomous: 1=yes, 0=no Measured from PCS claims data.
Gastrointestinal disorders (ulcers or gastrointestinal bleeding)	Dichotomous: 1=yes, 0=no Measured from PWP question 14.
Lung conditions (emphysema, bronchitis or asthma)	Dichotomous: 1=yes, 0=no Measured from PWP question 14.
Kidney disease	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
A history of falling	Dichotomous: 1=yes, 0=no Measured by PWP question 24.
Variables related to communication	
A previous adverse drug reaction	Dichotomous: 1=yes, 0=no Measured by PWP question 3, "Have you had a side effect due to a medication that caused you to stop that medication in the last 6 months?"
Four or more prescribers	Dichotomous: 1= 4 or more prescribers, 0=three or fewer prescribers Measured through the PCS outpatient prescription data.
Six or more prescription medications	Dichotomous: 1=six or more prescription medications, 0=five or fewer prescription medications The number of medications taken by a patient was measured by PWP question 24.
Four or more recorded diagnoses	Dichotomous: 1=four or more disease states, 0=three or fewer disease states. Measured by PWP question 14.
Variables related to biopsychosocial aspects of drug therapy	
Self-Assessment of poor health status	Dichotomous: 1=poor, 0=better than poor (other) Measured by PWP question one.
Trouble paying for medicines	Dichotomous: 1=yes, 0=no Measured by PWP question 23, "Do you have trouble paying for your medicines?"
Difficulty taking medications	Categories: 1= Difficult or Very difficult/can't do it, 0=Not difficult Measured by PWP question 31.

Table 4.4 Hypothesized Risk Factors and Their Measurement (Continued)

Hypothesized Risk Factor	Measurement
High Alcohol Consumption	Dichotomous: 1=yes, 0=no Measured by PWP question 11, "Do you often have more than 1 to 2 alcoholic drinks in a day?"
Patient belief that they are taking too many medications	Dichotomous: 1= Patient thinks they are on too many medications, 0= patient does not think they are on too many medications. Measured by PWP drug question 4, "How do you feel about the number of medications you are taking?"
Other variables of interest	
Female gender	Dichotomous: 1=female, 0=male Measured by the FHHS data.

Table 4.5 Additional Demographic Variables and Their Measurement

Additional Demographic Variable	Measurement
Arthritis	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Bladder/Bowel Control Problems	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Blind/Trouble Seeing, Even With Glasses	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Cancer (Non-skin)	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Congestive Heart Failure	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Coronary Disease	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Angina	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Myocardial Infarction	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Sciatica	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Deafness or Trouble Hearing	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Diabetes (High Blood Sugar)	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
High Blood Pressure	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Memory Problems (More Than Typical)	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Stroke	Dichotomous: 1=yes, 0=no Measured by PWP question 14.
Self-Assessment of Much Worse Health Status	Dichotomous: 1=much worse health status, 0=better than much worse Measured by PWP question 2.
Smoker	Dichotomous: 1=yes, 0=no Measured by PWP question 11.
Use of Six or More Over-The-Counter Medications (OTCs)	Dichotomous: 1=yes, 0=five or fewer OTCs Measured by PWP question 22.
Warfarin use	Dichotomous: 1=yes, 0=no Measured by PWP drug question 1.
Theophylline use	Dichotomous: 1=yes, 0=no Measured by PWP drug question 1.
Cimetidine use	Dichotomous: 1=yes, 0=no Measured by PWP drug question 1.
Phenytoin use	Dichotomous: 1=yes, 0=no Measured by PWP drug question 2.
Lives Alone	Dichotomous: 1=yes, 0=no Measured by PWP question 16.

Table 4.5 Additional Demographic Variables and Their Measurement (Continued)

Hypothesized Risk Factor	Measurement
Three or more hospitalizations in previous year	Dichotomous: 1=yes, 0=two or fewer hospitalizations Measured by PWP question 17.
Three or more ER visits in previous year	Dichotomous: 1=yes, 0=two or fewer ER visits Measured by PWP question 18.
Five or more MD clinic visits in previous year	Dichotomous: 1=yes, 0=four or fewer MD clinic visits Measured by PWP question 19.
Nursing home residence	Dichotomous: 1=yes, 0=no Measured by PWP question 20.
Use of durable medical equipment (oxygen, hospital bed, wheelchair, walker)	Dichotomous: 1=yes, 0=no Measured by PWP question 25.
Use of home health services (visiting nurse, physical therapy, homemaker/aide, adult day care)	Dichotomous: 1=yes, 0=no Measured by PWP question 26.

Factor Analysis

The second step of the statistical analysis was a factor analysis with a varimax (orthogonal) rotation of principal components. This was done on a random selection of 2500 patients from the study population, with the remaining 835 patients serving as a validation group. All 18 hypothesized risk factors were included in the factor analysis. After the factor analysis was completed, the number of factors identified and factor scores were studied. While factor analysis does make assumptions about the normality of the data, dichotomous data can be used with factor analysis with confidence, provided that sample sizes are large enough (greater than 200 observations)(Parry and McArdle, 1991).

The objective of the factor analysis was to (1) reduce the rather large number of hypothesized variables to a relatively small number of factors, or common traits, and (2) determine whether these factors matched the structure proposed in the semantic hierarchy. Factor analysis accomplishes the first objective by focusing on the part of the total variance that is shared by the variables, assuming that variables consist of common parts. The initial communality estimates were set as one. The results were kept in perspective as factor analysis is intended only to be used as a tool to help guide the researcher, not to be used without consideration of the conceptual framework being used and other factors (Maraun, 1996).

One of two approaches could be used, based on the results of the factor analysis. Had the factors matched the semantic hierarchy and shown to represent constructs with confidence, then principal component scores based on these factors would have been entered into a logistic regression model. However, because the factors did not match the semantic hierarchy and could not be shown to represent constructs with confidence, the risk factors from the first regression model were entered into another regression model with the additional variables, taking the factor analysis results into consideration.

Logistic Regression Models with Additional Variables

Additional logistic regression models were then run, with the risk factors from the first model entered a priori to adjust for their effects on PDRM. Other demographic variables were also allowed to enter the model to see if they added significantly to the prediction, based on statistical significance in a bivariate analysis between patients who did, and who did not, have PDRM. Because there was a theoretical basis for including the risk factors from the first model, it was felt that the final model for PDRM must include all of these risk factors, even if it explained less of the variance of PDRM. Thus, this process incorporated both statistical and theoretical criterion for deciding which terms to include in the model and this helped to focus attention on those variables that fit into the conceptual framework and that had the greatest independent effect on PDRM.

Following the creation of the final prediction model, a risk stratification system was developed. Patients were categorized according to the number of risk factors they had and a comparison was made between the patients with, and without, PDRM.

PDRM and Healthcare Resource Utilization

The final component of the methodology was to do another bivariate analysis to determine the relationship of PDRM to healthcare resource utilization. Each enrollee was classified as either having PDRM or not. Then, the utilization of health care resources was compared for the two groups.

CHAPTER 5
RESULTS

The results of this study will be presented in two parts. First, the results of the Delphi technique and the creation of the operational definitions of PDRM will be shared. Second, the results of the prediction models for PDRM and risk factors identified will be presented.

Delphi Technique - The Geriatric Medicine Expert Panel

As was discussed in the previous chapter, the Delphi technique was used in an attempt to generate consensus on PDRM. Two rounds were used until consensus was obtained. Appendix G contains the final list of consensus-approved operational definitions of PDRM. This appendix also includes all the comments made by the Geriatric Medicine Expert Panel members in either round 1 or round 2.

The expert panel agreed that 52 of the clinical scenarios presented to them were actual PDRMs. Table 5.1 shows the opinions of the panel members after round 1 and round 2. After round 1, the panel members' agreement with the clinical scenarios ranged from 60.4 percent to 97.9 percent. After round 2, the agreement ranged from 82.8 percent to 100 percent.

Initially, the panel members were presented with 47 unique clinical scenarios. One of these was listed twice, as a validity check, so the panel members were actually presented with 48 outcomes and patterns of care to evaluate. The validity check received the same score from all seven panel members for both rounds. After the first round, two clinical scenarios were rejected (received fewer than four "yes" votes). The panel members were given the opportunity to suggest

Table 5.1 Geriatric Medicine Expert Panel Results

Expert Number	Percentage (%) of clinical scenarios the expert felt were PDRMs after Round 1	Percentage (%) of clinical scenarios the expert felt were PDRMs after Round 2
1	95.8	100
2	97.9	82.8
3	79.2	89.7
4	60.4	91.4
5	79.2	87.9
6	77.1	91.4
7	97.9	94.8

other operational definitions of PDRMs and 12 were generated. One of these 12 new operational definitions was, in fact, a duplicate of a previous definition. These 12 new operational definitions were added to the remaining 46 operational definitions of PDRM and given to the panel members in round 2. After the second round, an additional four clinical scenarios were rejected, the two duplicates were removed, leaving 52 operational definitions of PDRM that were approved.

After round 2 there appeared to be overwhelming consensus on which clinical scenarios were actual PDRMs. Of the 52 clinical scenarios deemed to be PDRMs by the expert panel, 35 clinical scenarios had the agreement of all seven panel members, 15 clinical scenarios had the agreement of six out of the seven members, and two clinical scenarios had the agreement of five out of the seven members. There were no clinical scenarios that only had the agreement of four panel members. Table 5.2 lists shows how each panel member voted in round 2. Throughout the two round process, there were six clinical scenarios which did not have at least the support of four panel members. Table 5.3 lists these clinical scenarios that were rejected as being PDRMs.

Identification of Consensus-Approved Operational Definitions of PDRM in Database

The 52 PDRMs approved by the geriatric medicine expert panel were identified by first examining the study database for the outcomes related to the specific operational definitions of PDRM. Overall, 1005 patients with outcomes related to one of the 52 consensus-approved PDRMs were identified. Next, each patient with one of these outcomes was individually studied to determine whether the pattern of care associated with a PDRM was provided or not. The outcome and pattern of care matched a consensus-approved operational definition of PDRM in 158 cases. This represented 97 patients, as several patients had more than one specific

Table 5.2 Round 2 of the Delphi Technique

Number[a]	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5	Expert 6	Expert 7	Total "Yes"
1	Y	Y	Y	Y	Y	Y	Y	7
2	Y	Y	Y	Y	Y	Y	Y	7
3	Y	Y	Y	Y	Y	Y	Y	7
4	Y	Y	Y	Y	Y	Y	Y	7
5	Y	Y	Y	Y	Y	Y	Y	7
6	Y	Y	Y	Y	Y	Y	Y	7
7	Y	Y	Y	Y	Y	Y	Y	7
8	Y	Y	Y	Y	Y	Y	Y	7
9	Y	Y	Y	Y	Y	Y	Y	7
10	Y	Y	Y	Y	Y	Y	Y	7
11	Y	Y	Y	Y	Y	Y	Y	7
12	Y	Y	Y	Y	Y	Y	Y	7
13	Y	Y	Y	Y	Y	Y	Y	7
14	Y	Y	Y	Y	Y	Y	Y	7
15	Y	Y	Y	Y	Y	Y	Y	7
16	Y	Y	Y	Y	Y	Y	Y	7
17	Y	Y	Y	Y	Y	Y	Y	7
18	Y	Y	Y	Y	Y	Y	Y	7
19	Y	Y	Y	Y	Y	Y	Y	7
20	Y	Y	Y	Y	Y	Y	Y	7
21	Y	Y	Y	Y	Y	Y	Y	7
22	Y	Y	Y	Y	Y	Y	Y	7
23	Y	Y	Y	Y	Y	Y	Y	7
24	Y	Y	Y	Y	Y	Y	Y	7
25	Y	Y	Y	Y	Y	Y	Y	7
26	Y	Y	Y	Y	Y	Y	Y	7
27	Y	Y	Y	Y	Y	Y	Y	7
28	Y	Y	Y	Y	Y	Y	Y	7
29	Y	Y	Y	Y	Y	Y	Y	7
30	Y	Y	Y	Y	Y	Y	Y	7
31	Y	Y	Y	Y	Y	Y	Y	7
32	Y	Y	Y	Y	Y	Y	Y	7
33	Y	Y	Y	Y	Y	Y	Y	7
34	Y	Y	Y	Y	Y	Y	Y	7
35	Y	Y	Y	Y	Y	Y	Y	7
36	Y	Y	Y	Y	Y	N	Y	6
37	Y	N	Y	Y	Y	Y	Y	6
38	Y	N	Y	Y	Y	Y	Y	6
39	Y	N	Y	Y	Y	Y	Y	6
40	Y	Y	N	Y	Y	Y	Y	6
41	Y	Y	Y	Y	N	Y	Y	6
42	Y	N	Y	Y	Y	Y	Y	6

Table 5.2 Round 2 of the Delphi Technique (Continued)

Number[a]	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5	Expert 6	Expert 7	Total "Yes"
43	Y	Y	N	Y	Y	Y	Y	6
44	Y	Y	N	Y	Y	Y	Y	6
45	Y	Y	Y	Y	N	Y	Y	6
46	Y	Y	Y	N	Y	Y	Y	6
47	Y	Y	Y	Y	Y	N	Y	6
48	Y	N	Y	Y	Y	Y	Y	6
49	Y	Y	Y	Y	N	Y	Y	6
50	Y	N	Y	Y	Y	Y	Y	6
51	Y	Y	N	Y	N	Y	Y	5
52	Y	N	Y	Y	Y	Y	N	5
53[b]	Y	N	Y	N	N	N	Y	3
54[b]	Y	Y	N	N	Y	N	N	3
55[b]	Y	N	N	N	N	Y	N	2
56[b]	Y	N	Y	N	N	N	Y	3
57[c]	Y	Y	Y	Y	Y	Y	Y	7
58[d]	Y	Y	Y	Y	Y	Y	Y	7

[a] See Appendix G for a description of the PDRM
[b] Rejected as an operational definition of PDRM
[c] Duplicate – same as PDRM #2
[d] Duplicate – same as PDRM #17

Table 5.3 Clinical Scenarios That Were Rejected As Preventable Drug-Related Morbidities

Clinical Scenario (Outcome and Pattern of Care)
Outcome: Fall and/or hip fracture and/or other bone fracture and/or bone break Pattern of care: 1. Use of an anti-parkinsonian agent (e.g.; levodopa, bromocriptine, Benztropine, etc.)
Outcome: Major and/or minor hemorrhagic event Pattern of care: 1. Use of SQ heparin 2. PTT not done at least every month
Outcome: Digoxin toxicity Pattern of care: 1. Use of digoxin 2. BUN/serum creatinine not done at least every 6 months 3. Digoxin level not done at least every 6 months
Outcome: Fall and/or hip fracture and/or other bone fracture and/or bone break Pattern of care: 1. Use of a nitrate (e.g.; isosorbide)
Outcome: Acute renal failure and/or renal insufficiency Pattern of care: 1. Use of allopurinol 2. BUN/serum creatinine not done at least every 6 months
Outcome: Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization Due to asthma Pattern of care: 1. Diagnosis of asthma 2. Use of theophylline 3. Drug level not done at least every 6 months

operational definition of PDRM. Table 5.4 shows the individual breakdown of each of the 52 consensus-approved operational definitions of PDRM.

As previously mentioned, many patients experienced more than one specific operational definition of PDRM. Table 5.5 shows the number of PDRMs each patient had, along with the number of specific outcomes these PDRM represented. This distinction is important to make because some patients met the criteria for more than one PDRM, but these PDRMs shared the same outcome (e.g. there are several PDRMs related to major/minor hemorrhagic events with different patterns of care).

Validation of Operational Definitions of Preventable Drug-Related Morbidity

Pharmacist agreement with the PDRM classification assigned by the operational definitions of PDRM was acceptable, although it varied for the two specific operational definitions of PDRM included in the analysis. Tables 5.6 and 5.7 show the individual panel members' classification for each patient. One patient chart for the hyperglycemia outcome and four patient charts for the secondary myocardial infarction outcome could not be located and they were not included in the final analysis.

Overall, the sensitivity of the two specific operational definitions of PDRM was 87.5 percent and the specificity was 73.5 percent (Table 5.8). For the hyperglycemia outcome, the sensitivity was 93.3 percent and the specificity was 81.3 percent (Table 5.9). For this outcome, the chart abstracts had to be administered a second time to the Chart Abstract Reviewer Panel because not all panel members followed the initial instructions, as will be discussed in the next chapter. For the secondary myocardial infarction outcome, the sensitivity was 82.4 percent and the specificity was 66.7 percent (Table 5.10).

Table 5.4 Patients with Outcomes and PDRM

PDRM Number [a]	Number of Patients with Outcome (%) (n=1005)	Number of Patients with PDRM (%) (n=97) [b]	Percentage (%) of Patients with the outcome who have PDRM	PDRM Number [a]	Number of Patients with Outcome (%) (n=1005)	Number of Patients with PDRM (%) (n=97) [b]	Percentage (%) of Patients with the outcome who have PDRM
1	28 (2.8)	8 (8.2)	28.6	27	14 (1.4)	0 (0.0)	0
2	24 (2.4)	6 (6.2)	25.0	28	45 (4.5)	2 (2.1)	4.4
3	0 (0.0)	0 (0.0)	0	29	28 (2.8)	3 (3.1)	10.7
4	7 (0.7)	1 (1.0)	14.3	30	13 (1.3)	0 (0.0)	0
5	24 (2.4)	0 (0.0)	0	31	2 (0.2)	0 (0.0)	0
6	3 (0.3)	1 (1.0)	33.3	32	7 (0.7)	0 (0.0)	0
7	17 (1.7)	0 (0.0)	0	33	39 (3.9)	2 (2.1)	5.1
8	24 (2.4)	0 (0.0)	0	34	16 (1.6)	7 (7.2)	43.8
9	0 (0.0)	0 (0.0)	0	35	1 (0.1)	0 (0.0)	0
10	0 (0.0)	0 (0.0)	0	36	32 (3.2)	8 (8.2)	25.0
11	45 (4.5)	4 (4.1)	8.9	37	32 (3.2)	6 (6.2)	18.8
12	28 (2.8)	2 (2.1)	7.1	38	2 (0.2)	1 (1.0)	50.0
13	27 (2.7)	0 (0.0)	0	39	3 (0.3)	0 (0.0)	0
14	2 (0.2)	0 (0.0)	0	40	0 (0.0)	0 (0.0)	0
15	2 (0.2)	0 (0.0)	0	41	14 (1.4)	12(12.4)	85.7
16	46 (4.6)	4 (4.1)	8.7	42	31 (3.1)	3 (3.1)	9.7
17	7 (0.7)	1 (1.0)	14.3	43	31 (3.1)	3 (3.1)	9.7
18	24 (2.4)	10(10.3)	41.7	44	7 (0.7)	0 (0.0)	0
19	0 (0.0)	0 (0.0)	0	45	16 (1.6)	0 (0.0)	0
20	0 (0.0)	0 (0.0)	0	46	24 (2.4)	0 (0.0)	0
21	32 (3.2)	18(18.6)	56.3	47	31 (3.1)	6 (6.2)	19.4
22	45 (4.5)	5 (5.2)	11.1	48	24 (2.4)	6 (6.2)	25.0
23	0 (0.0)	0 (0.0)	0	49	31 (3.1)	1 (1.0)	3.2
24	39 (3.9)	24(24.7)	61.5	50	42 (4.2)	2 (2.1)	4.8
25	12 (1.2)	0 (0.0)	0	51	32 (3.2)	10(10.3)	31.3
26	45 (4.5)	1 (1.0)	2.2	52	7 (0.7)	1 (1.0)	14.3

[a] See Appendix G for the description of the PDRM.

[b] Adds up to over 100 percent because some patients had more than one operational definition of PDRM.

Table 5.5 Number of PDRMs and Specific Outcomes by Individual Patients

Patient Category	Number of Patients with PDRM (%) n=97
1 case of PDRM with 1 specific outcome	61 (62.9)
2 cases of PDRM with 1 specific outcome	12 (12.4)
2 cases of PDRM with 2 specific outcomes	6 (6.2)
3 cases of PDRM with 1 specific outcome	4 (8.2)
3 cases of PDRM with 2 specific outcomes	8 (8.2)
3 cases of PDRM with 3 specific outcomes	0 (0.0)
4 cases of PDRM with 1 specific outcome	0 (0.0)
4 cases of PDRM with 2 specific outcomes	3 (3.1)
4 cases of PDRM with 3 specific outcomes	0 (0.0)
4 cases of PDRM with 4 specific outcomes	2 (2.1)
5 cases of PDRM with 1 specific outcome	0 (0.0)
5 cases of PDRM with 2 specific outcomes	0 (0.0)
5 cases of PDRM with 3 specific outcomes	1 (1.0)
5 cases of PDRM with 4 specific outcomes	0 (0.0)
5 cases of PDRM with 5 specific outcomes	0 (0.0)

Table 5.6 Chart Abstract Reviewer Panel Results for Hyperglycemia with no Regular HgA1c Monitoring

Pt #	RPh #1	RPh #2	RPh #3	RPh #4	RPh #5	Total "yes"	PDRM according to definition
1	Y	Y	Y	Y	Y	5	Y
2	Y	Y	Y	Y	Y	5	Y
3	N	N	N	N	Y	1	N
4	Y	Y	Y	Y	Y	5	Y
5	Y	N	N	Y	N	2	N
6	Y	N	N	N	Y	2	N
7	Y	Y	Y	Y	Y	5	Y
8	Y	Y	N	Y	Y	4	Y
9	Y	Y	N	Y	Y	4	Y
10	Y	Y	Y	Y	Y	5	Y
11	N	N	N	N	Y	1	N
12	N	N	N	N	N	0	N
13	N	N	N	N	N	0	N
14	Y	Y	Y	Y	Y	5	Y
15	Y	Y	Y	Y	Y	5	Y
16	N	N	N	N	N	0	N
17	N	Y	N	Y	N	2	N
18	Y	Y	Y	Y	N	4	Y
19	N	Y	N	Y	N	2	N
20	N	Y	N	Y	N	2	Y
21	Y	Y	Y	Y	Y	5	N
22	N	Y	N	N	Y	2	Y
23	N	N	N	N	Y	1	N
24 *							Y
25	N	N	Y	N	N	1	N
26	Y	Y	Y	Y	Y	5	Y
27	N	Y	N	N	N	1	N
28	Y	Y	Y	Y	Y	5	Y
29	Y	Y	Y	Y	Y	5	Y
30	Y	N	N	Y	N	2	Y
31	Y	Y	Y	Y	Y	5	Y
32	N	N	N	N	Y	1	N

* Chart abstract could not be done because patient chart could not be located.

Table 5.7 Chart Abstract Reviewer Panel Results: Secondary Myocardial Infarction in Patients Without ASA and/or Beta-Blocker Use

Pt #	RPh #1	RPh #2	RPh #3	RPh #4	RPh #5	Total "Yes"	PDRM according to definition
1	N	N	N	N	N	0	N
2	Y	Y	Y	Y	N	4	N
3	N	N	N	N	Y	1	N
4	Y	Y	N	Y	N	3	Y
5	Y	Y	Y	Y	Y	5	Y
6	N	Y	Y	N	N	2	N
7	Y	N	N	Y	N	2	N
8	N	N	Y	Y	Y	3	N
9	Y	Y	Y	Y	Y	5	Y
10*							Y
11	Y	Y	Y	N	Y	4	Y
12	Y	Y	Y	Y	Y	5	Y
13	Y	N	N	Y	Y	3	Y
14	Y	Y	Y	Y	Y	5	Y
15	Y	Y	Y	Y	Y	5	N
16	Y	N	N	Y	Y	3	Y
17	Y	Y	Y	Y	Y	5	Y
18	Y	Y	Y	Y	Y	5	Y
19	Y	N	Y	N	Y	3	Y
20	N	N	N	Y	Y	2	N
21	N	N	N	Y	N	1	N
22*							Y
23	Y	Y	Y	Y	Y	5	Y
24	Y	Y	Y	Y	Y	5	Y
25	Y	Y	Y	Y	Y	5	Y
26*							Y
27*							Y
28	Y	Y	Y	N	N	3	Y
29	N	Y	N	Y	Y	2	Y
30	Y	Y	Y	Y	N	4	Y
31	N	N	N	Y	N	1	N
32	Y	N	Y	Y	Y	4	Y
33	Y	N	Y	Y	N	3	N
34	Y	Y	Y	Y	Y	5	Y
35	Y	N	Y	Y	Y	4	N
36	N	N	N	Y	Y	2	N
37	Y	Y	Y	Y	Y	5	Y
38	N	Y	N	Y	N	2	N
39	N	N	N	Y	N	1	N

* Chart abstract could not be done because patient chart could not be located.

Table 5.8 Sensitivity and Specificity for Both of the Operational Definitions of PDRM

		Operational Definition of PDRM	
		Yes	No
True PDRM	Yes	28	4
	No	9	25

Sensitivity was calculated as [28/(28+4)] x 100 = 87.5 percent.
Specificity was calculated as [25/(25+9)] x 100 = 73.5 percent.
True PDRM (Yes) = Four or more of the panel members classified as PDRM,
True PDRM (No) = Four or more of the panel members classified as non-PDRM,
Operational definition of PDRM (Yes) = Classified as a PDRM by the operational definition,
Operational definition of PDRM (No) - Classified as a non-PDRM by the operational definition.

Table 5.9 Sensitivity and Specificity of the Operational Definition of PDRM (Hyperglycemia Outcome)

		Operational Definition of PDRM	
		Yes	No
True	Yes	14	1
PDRM	No	3	13

Sensitivity was calculated as [14/(14+1)] x 100 = 93.3 percent.
Specificity was calculated as [13/(13+3)] x 100 = 81.3 percent.
True PDRM (Yes) = Four or more of the panel members classified as PDRM,
True PDRM (No) = Four or more of the panel members classified as non-PDRM,
Operational definition of PDRM (Yes) = Classified as a PDRM by the operational definition,
Operational definition of PDRM (No) - Classified as a non-PDRM by the operational definition.

Table 5.10 Sensitivity and Specificity of the Operational Definition of PDRM (Secondary Myocardial Infarction Outcome)

		Operational Definition of PDRM	
		Yes	No
True	Yes	14	3
PDRM	No	6	12

Sensitivity was calculated as [14/(14+3)] x 100 = 82.4 percent.
Specificity was calculated as [12/(12+6)] x 100 = 66.7 percent.
True PDRM (Yes) = Four or more of the panel members classified as PDRM,
True PDRM (No) = Four or more of the panel members classified as non-PDRM,
Operational definition of PDRM (Yes) = Classified as a PDRM by the operational definition,
Operational definition of PDRM (No) - Classified as a non-PDRM by the operational definition.

The agreement among the five pharmacists in classifying the patients into those with PDRM, and those without PDRM, was acceptable. Fleiss's measure of overall agreement for the hyperglycemia patients was 0.652, for the secondary myocardial infarction patients it was 0.674 and overall it was 0.664. Therefore, if a patient was selected at random and classified as either having, or not having, PDRM by a randomly selected panel member, a second randomly selected panel member would agree with the first panel member 66.4 percent of the time.

Therefore, because of the consensus reached by the Geriatric Medicine Expert Panel and the high sensitivity and specificity of the two validated operational definitions, research assumption A1A could be met: valid operational definitions of PDRM can be developed by a panel of geriatric medicine experts.

Phase II: Identification of Risk Factors for PDRM

Phase II involved the identification of risk factors for PDRM. First, the results of the statistical analyses used to identify the risk factors will be presented. Second, the results related to the hypothesis for each risk factor will be shown. Third, the results related to the hypothesis of general risk factors and drug (and disease) specific risk factors will be presented. Finally, the relationship between PDRM and healthcare resource utilization will be discussed.

Logistic Regression with all 18 Hypothesized Risk Factors

In order to test the first set of hypotheses regarding possible risk factors for PDRM, a logistic regression analysis was performed. A forward inclusion procedure was used with the entry level set at p=0.05.

A five-variable risk model was produced (Table 5.11). This model indicates that patients with *four or more recorded diagnoses* were 2.93 times more likely to have PDRM than those with three or fewer diseases. Patients with *antihypertensive drug use* are at a much greater risk

Table 5.11 Logistic Regression Model With All 18 Hypothesized Variables

Variable	Parameter Estimate (b)	Standard Error (SE)	Chi-Square Probability	Odds Ratio	95 Percent Confidence Interval
Four or more prescribers	0.2683	0.0602	0.0001	1.308	1.162-1.472
Four or more recorded diagnoses	1.0758	0.2475	0.0001	2.932	1.805-4.763
Female gender	-0.6633	0.2393	0.0056	0.515	0.823-0.322
Antihypertensive drug use	0.7023	0.2787	0.0118	2.018	1.156-3.524
Six or more prescription medications	0.6525	0.2942	0.0266	1.920	1.079-3.418
Equation Constant	-4.6958	0.2758	0.0001	-	-

(2.02 times) for having PDRM, as are patients taking *six or more prescription medications* (1.92 times). One other variable, *four or more prescribers*, also placed patients at a greater risk (1.31 times) for developing a PDRM. Finally, the odds ratio for *female gender* was less than one (0.52), meaning that females were at a far lower risk of developing PDRM than males. None of the 95 percent confidence intervals for the odds ratios contained 1, and the confidence intervals were quite small.

The fit of this prediction model appears to be quite good. To measure how well the estimated model fits the data, two times the log of the likelihood (-2LL) is used. The difference between the -2LL for the intercept (constant) only and for the constant plus the covariates (variables) is referred to as the G statistic (Menard, 1995). Here the G statistic, which tests whether the information about the independent variables allows one to make a better prediction of the dependent variable, is significant (chi square = 101.402 with 5 df, p =0.0001). Therefore, addition of these variables did significantly increase the model chi square. The Score statistic, which tests the statistical significance of the combined effects of the independent variables in the model, confirms these findings (Menard, 1995). It is significant as well (chi square = 130.166 with 5 df, p=0.0001). Therefore, overall, the fit of the model is good as evidenced by these tests.

The amount of variance explained by the prediction model is also quite good. While R^2 is not recommended for use in logistic regression, an analogue called R_L^2 has been proposed (Menard, 1995). This statistic measures the proportional reduction on chi-square and it varies between 0 and 1 (where 1= the model predicts the dependent variable perfectly) (Menard, 1995). For this prediction model, the R_L^2 is 0.562.

Other attributes of this model suggest that it is free of multicollinearity and that it is quite accurate. Table 5.12 shows the correlation matrix for the final variables in the model. Overall, the correlations (pairwise relationships) between the variables are quite low. Only two correlations were greater than +/- 0.20: *four or more prescribers* and *antihypertensive drug use*

Table 5.12 Correlation Matrix for Significant Variables in Regression Model With All 18 Hypothesized Variables

	Con-stant	*Female Gender*	*Four or more recorded diagno-ses*	*Six or more prescription medications*	*Four or more prescribers*	*Antihyper-tensive drug use*
Constant	1.00					
Female Gender	-0.3520	1.00				
Four or more recorded diagnoses	-0.2899	0.0274	1.00			
Six or more prescription medications	0.0524	-0.0323	0.2965	1.00		
Four or more prescribers	-0.3626	0.0042	0.0500	0.1556	1.00	
Antihyper-tensive drug use	-0.4854	0.0224	0.0894	0.0894	0.2995	1.00

(0.2995), and *four or more recorded diagnoses* and *six or more prescription medications* (0.2965). A backward elimination procedure was also performed, which yielded identical results. The classification accuracy of the model is quite good, as determined by the jack-knife method (Table 5.13). The sensitivity was 56.1 percent, the specificity was 86.8 percent, the positive predictive value was 11.5 percent and the negative predictive value was 98.5 percent.

Factor Analysis

The second step of the statistical analysis was a factor analysis (orthogonal) of principal components. This was done on a random selection of 2500 patients out of the 3365 patients in the study population, with the remaining 835 patients serving as the validation group. This factor analysis included all 18 hypothesized risk factors.

The factor analysis suggested that there are six factors. Several things were considered when coming to this conclusion. There were seven factors with eigenvalues greater than one, although the eigenvalues down to the tenth factor were all quite large (the eigenvalue for factor 10 was 0.9176). Cattell's Scree Plot showed a large separation between factors 4 and 5, a smaller separation between factors 6 and 7 and then another separation between factors 10 and 11. To avoid underextracting the number of factors, up to ten factors were specified in the factor analysis. Great factor stability was observed in the factor analyses done with ten to six specified factors. Therefore, six factors were chosen for simplicity and to avoid the dangers of overextraction in factor analysis (Fava and Velicer, 1992).

The results of the factor analysis with six factors can be seen in Table 5.14. These six factors were subjected to a varimax (orthogonal) rotation. Several other results seem to support that the factors seen in Table 5.14 are reliable. First, the final communality estimates, which are squares of the factor patterns, were at least 0.50 (acceptable) for all the variables except for lung

Table 5.13 Classification Table for the Regression Model with the 18 Hypothesized Variables

		Predicted	
		Yes	No
Actual	Yes	46	36
	No	354	2318

Sensitivity was calculated as [46/(46+36)] x 100 = 56.1 percent.
Specificity was calculated as [2318/(2318+354)] x 100 = 86.8 percent.
Positive Predictive Value [46/(46+354)] x 100 = 11.5 percent.
Negative Predictive Value [2318/(2318+36)] x 100 = 98.5 percent
Overall Percentage accuracy in Classification [2364/(390+2364)] x 100 = 85.8 percent

Table 5.14 Rotated Factor Matrix - Varimax

Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
Kidney disease	.83					
Gastrointestinal disorders	.79					
Four or more recorded diagnoses	.71					
Lung conditions	.60					
Four or more prescribers		.78				
Antihypertensive drug use		.72				
Antidepressant drug use		.49				
Six or more prescription medications			.66			
Digoxin use			.53			
Self-assessment of poor health status			.51			
A history of falling				.70		
Difficulty taking drugs				.67		
Long-acting benzodiazepine use				.40		
Patient belief that they are taking too many medications					.68	
Trouble paying for medications					.46	
A previous adverse drug reaction					.43	
High alcohol consumption						.70
Female gender						-.71
Eigenvalue	2.58	1.57	1.37	1.17	1.07	1.05

Only factor scores greater than +/- 0.40 are shown.

disease (0.40). Second, a factor analysis done with a Harris Kaiser rotation (oblique) yielded almost identical results, given that the factors were in different order (Table 5.15). In a Harris Kaiser rotation the rotated factors become correlated and sometimes produce more useful factor patterns. In cases like this, where the Harris Kaiser rotation yields similar results to the orthogonal rotation, it can be concluded that the correlations among the factors are minimal and the orthogonal rotation may be used for interpretation (Pedhazur and Schmelkin, 1991). Third, the validation group of 835 patients also yielded very similar results (Table 5.16).

Constructs could not be assigned to the six factors with certainty. While the factor groupings do not seem to relate to definite constructs in the medication use system, the variables that were grouped together in the same factor do appear reasonable. Because of this inability to assign each factor a construct, factor scores were not used in a logistic regression equation. Instead, the five risk factors identified in the regression model with all 18 hypothesized risk factors were used. Of the five risk factors, one was contained in factor 1 (*four or more recorded diagnoses*), two were contained in factor 2 (*four or more prescribers* and *antihypertensive drug use*), one was contained in factor 3 (*six or more prescription medications*), and one was contained in factor 6 (*female gender*). There was no risk factor contained in factors 4 or 5. A more detailed discussion of the factor analysis is contained in the next chapter.

Bivariate Analysis

A bivariate analysis was conducted for the purpose of identifying variables in the study database, other than the 18 hypothesized variables, that might be associated with PDRM. These other variables represent a wide variety of demographics related to healthcare (diseases, history of healthcare resource utilization, medications, etc.) and were not chosen because of any empirical or theoretical evidence that they are risk factors for PDRM. In comparing patients

Table 5.15 Rotated Factor Matrix - Harris-Kaiser

Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
High alcohol consumption	.71					
Female gender	-.71					
Four or more prescribers		.80				
Antihypertensive drug use		.74				
Antidepressant drug use		.45				
Kidney disease			.82			
Gastrointestinal disorders			.79			
Four or more recorded diagnoses			.73	.46		
Lung conditions			.61			
Six or more prescription medications				.68		
Digoxin use				.56		
Self-assessment of poor health status				.52		
Patient belief that they are taking too many medications					.69	
A previous adverse drug reaction					.49	
Trouble paying for medications					.45	
A history of falling						.70
Difficulty taking medications						.67
Long-acting benzodiazepine use						.40
Eigenvalue	2.58	1.57	1.37	1.17	1.07	1.05

Only factor scores greater than +/- 0.40 are shown.

Table 5.16 Rotated Factor Matrix - Varimax Validation Group

Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
Kidney disease	.82					
Gastrointestinal disorders	.78					
Four or more recorded diagnoses	.76					
Lung conditions	.61					
Antihypertensive drug use		.81				
Four or more prescribers		.75				
Antidepressant drug use		.62				
Self-assessment of poor health status			.62			
Digoxin use			.62			
Six or more prescription medications			.42			
Female gender				-.63		
Patient belief that they are taking too many medications				.59		
High alcohol consumption				.48		
A history of falling					.69	
Difficulty taking medications					.67	
A previous adverse drug reaction						.73
Trouble paying for medications						.54
Eigenvalue	2.58	1.57	1.37	1.17	1.07	1.05

Only factor scores greater than +/- 0.40 are shown.

with, and without PDRM, a chi-square test was used to test for any significant difference in the variables. If the expected frequency was less than five in either cell, then the Fisher's Exact Test was used. The results of the bivariate analysis for the original 18 hypothesized variables can be seen in Table 5.17. The results of the analysis for the 28 additional demographic variables can be seen in Table 5.18. If the chi square value for a variable was significantly associated with PDRM in the bivariate analysis ($p<0.05$) then it was included in following regression model.

Logistic Regression Models with Additional Demographic Variables

It was thought that there might be some additional demographic variables that are risk factors for PDRM. If a variable was significantly associated with PDRM in the bivariate analysis ($p<0.05$) then it was included in the regression model along with the five variables that were identified as risk factors in the original model. A forward inclusion procedure was again used with the entry level set at $p=0.05$.

A seven-variable risk model was produced (Table 5.19). As before, patients with *four or more recorded diagnoses* were more likely to have PDRM (odds ratio = 2.32), as well as those with *antihypertensive drug use* (odds ratio = 2.29), and those with *four or more prescribers* (odds ratio = 1.27). Also, the odds ratio for *female gender* was again less than one (0.60), meaning that females were at a far lower risk of developing PDRM than males. New variables included in the final model were *angina* (odds ratio = 1.87), *three or more hospitalizations in the previous year* (odds ratio = 2.02), and *use of durable medical equipment* (odds ratio = 2.23). *Six or more prescription medications* was not contained in this model. None of the 95 percent confidence intervals for the odds ratios contained 1, and the confidence intervals were quite small.

The fit of this prediction model appears to be quite good. The G statistic is significant (chi square = 126.032 with 7 df, $p =0.0001$). Therefore, the addition of these seven explanatory variables did significantly increase the model chi square. The Score statistic confirms these

Table 5.17 Bivariate Analysis of Patients With, and Without, PDRM Categorized by Hypothesized Variables

Variable	No. (%) with PDRM (n=97)	No. (%) without PDRM (n=3268)	P value
Digoxin use	12 (12.4)	212 (6.5)	0.022[a]
Antidepressant drug use	15 (15.5)	235 (7.2)	0.002[b]
Long-acting benzodiazepine use	2 (2.1)	80 (2.5)	0.808[d]
Antihypertensive drug use	74 (76.3)	1375 (42.1)	0.001[c]
Gastrointestinal disorders	15 (15.5)	182 (5.6)	0.001[c]
Lung conditions	21 (21.7)	436 (13.4)	0.019[a]
Kidney disease	12 (12.4)	120 (3.7)	0.001[c]
A history of falling	4 (4.2)	78 (2.4)	0.299[d]
Four or more prescribers	32 (33.0)	388 (11.9)	0.001[c]
Six or more prescription medications	24 (25.5)	235 (7.3)	0.001[c]
Four or more recorded diagnoses	56 (57.7)	667 (20.4)	0.001[c]
A previous adverse drug reaction	9 (9.8)	405 (13.0)	0.362
High alcohol consumption	6 (6.5)	222 (7.1)	0.822
Self-assessment of poor health status	8 (8.3)	74 (2.3)	0.001[c]
Trouble paying for medications	8 (8.5)	158 (5.0)	0.126
Difficulty taking medications	2 (2.2)	51 (1.7)	0.668[d]
Patient belief that they are taking too many medications	10 (10.6)	186 (5.9)	0.055
Female gender	42 (43.3)	1808 (55.3)	0.019[a]

[a] Significance difference in variable between patients with, and without, PDRM, $p < 0.05$
[b] Significance difference in variable between patients with, and without, PDRM, $p < 0.01$
[c] Significance difference in variable between patients with, and without, PDRM, $p < 0.001$
[d] Probability value for Fisher's Exact Test

Table 5.18 Bivariate Analysis of Patients With, and Without, PDRM, Categorized by Additional Demographic Variables

Variable	No. (%) with PDRM (n=97)	No. (%) without PDRM (n=3268)	P value
Arthritis	61 (62.9)	1497 (45.8)	0.001[c]
Bladder/Bowel Disease	30 (30.9)	560 (17.1)	0.001[c]
Vision Problems	24 (24.7)	323 (9.9)	0.001[c]
Cancer (Non-skin)	20 (20.6)	314 (9.6)	0.001[c]
Heart Failure	19 (19.6)	189 (5.8)	0.001[c]
Coronary Disease	32 (33.0)	384 (11.6)	0.001[c]
Angina	29 (29.9)	280 (8.6)	0.001[c]
Myocardial Infarction	10 (10.3)	148 (4.5)	0.008[b]
Sciatica	32 (33.0)	666 (20.4)	0.003[b]
Deafness	35 (36.1)	708 (21.7)	0.001[c]
Diabetes	34 (35.1)	445 (13.6)	0.001[c]
High Blood Pressure	58 (59.8)	1202 (36.8)	0.001[c]
Memory Problems	20 (20.6)	274 (8.4)	0.001[c]
Stroke	19 (19.6)	191 (5.9)	0.001[c]
Much Worse Health Status	2 (2.1)	27 (0.8)	0.209[d]
Smoker	7 (7.5)	225 (7.1)	0.882
Use of six or more OTCs	1 (1.1)	14 (0.4)	0.357[d]
Warfarin use	7 (7.2)	110 (3.4)	0.041[a]
Theophylline use	3 (3.1)	94 (2.9)	0.758[d]
Cimetidine use	8 (8.3)	149 (4.6)	0.090
Phenytoin use	0 (0.0)	12 (0.4)	1.000[d]
Lives Alone	9 (9.5)	328 (10.3)	0.796
Three or more hospitalizations in previous year	17 (18.1)	120 (3.7)	0.001[c]
Three or more ER visits in previous year	4 (4.3)	26 (0.8)	0.001[c,d]
Five or more MD clinic visits in previous year	68 (71.6)	1413 (43.8)	0.001[c]
Nursing home residence	2 (2.1)	28 (0.9)	0.209[d]
Use of durable medical equipment	22 (23.2)	219 (6.8)	0.001[c]
Use of home health care services	6 (6.3)	49 (1.5)	0.001[c]

[a] Significance difference in variable between patients with, and without, PDRM, $p < 0.05$
[b] Significance difference in variable between patients with, and without, PDRM, $p < 0.01$
[c] Significance difference in variable between patients with, and without, PDRM, $p < 0.001$
[d] Probability value for Fisher's Exact Test

Table 5.19 Logistic Regression Model Including Additional Demographic Variables

Variable	Parameter Estimate (b)	Standard Error (SE)	Chi Square Probability	Odds Ratio	95 Percent Confidence Interval
Four or more prescribers	0.2387	0.0590	0.0001	1.270	1.131-1.425
Four or more recorded diagnoses	0.8428	0.2621	0.0013	2.323	1.390-3.883
Antihypertensive drug use	0.8271	0.2746	0.0026	2.287	1.335-3.917
Female gender	-0.5105	0.2276	0.0055	0.600	0.384-0.937
Use of durable medical equipment	0.8021	0.2887	0.0249	2.230	1.266-3.927
Angina	0.6230	0.2812	0.0267	1.865	1.074-3.235
Three or more hospitalizations in the previous year	0.7029	0.3325	0.0345	2.020	1.053-3.875
Equation Constant	-4.9206	0.2739	0.0001	-	-

findings (chi square = 174.511 with 7 df, p=0.0001). Therefore, overall, the fit of the model is good as evidenced by these tests.

The amount of variance explained by the prediction model is slightly greater then for the regression model with the only the 18 hypothesized risk factors. For this prediction model, the R_L^2 is 0.581.

This regression model also seems to be free of multicollinearity. Table 5.20 shows the correlation matrix for the final variables in the model. Overall, the correlations between the variables are quite low, with the highest one being between *four or more recorded diagnoses* and *angina* (0.42594). A backward elimination procedure was also performed, which yielded identical results.

Although this last model did explain slightly more variance ($R_L^2 = 0.581$) than the original model ($R_L^2 = 0.562$), the increased complexity of the new model and the elimination of one of the original risk factors from the first model (*six or more prescription medications*) were cause for further analysis. Therefore, an attempt was made to determine the relationship between *six or more prescription medications* and the new risk factors since *six or more prescription medications* dropped from this last model.

Three regression models were performed with the five risk factors from the first model and each of the three new risk factors from the last model. A simultaneous regression approach, rather than forward inclusion or backward elimination techniques, were used as the intent was to keep all six variables in the final model. *Six or more prescription medications* was not a statistically significant predictor of PDRM in any of the three models. The correlation between *six or more prescription medications* and the three new risk factors was relatively small (*six or more prescription medications* and *use of durable medical equipment* = 0.2562, *six or more prescription medications* and *angina* =0.0842, and *six or more prescription medications* and *three or more hospitalizations in the previous year* = 0.1002). The parameter estimate for *six or more prescription medications* remained stable in all three models. The odds ratio for *six or more prescription medications* was also relatively stable in all three models and it was nearly as

Table 5.20 Correlation Matrix for Significant Variables in Regression Model with Additional Variables

	Constant	*Female gender*	*Four or more recorded diagnoses*	*Four or more prescribers*	*Antihypertensive drug use*	*Angina*	*Three or more hospitalizations in the previous year*	*Use of durable medical equipment*
Constant	1.00							
Female gender	-0.3591	1.00						
Four or more recorded diagnoses	-0.2268	0.0202	1.00					
Four or more prescribers	-0.3330	-0.0056	0.0597	1.00				
Antihypertensive drug use	-0.4946	0.0146	0.0767	0.2993	1.00			
Angina	-0.0367	-0.0028	0.4259	0.0043	0.0624	1.00		
Three or more hospitalizations in the previous year	-0.0255	0.0052	0.0984	0.1336	0.0301	0.0419	1.00	
Use of durable medical equipment	-0.0564	-0.0130	0.2252	0.0528	0.0274	0.1131	0.1702	1.00

large as it was in the original model (OR = 1.463, 1.594, and 1.640 in these three models, and OR=1.920 in the original model).

Finally, to further clarify the relationship of *six or more prescription medications* and these three new risk factors, a factor analysis (orthogonal rotation) of principal components was performed with the five original risk factors and the three new risk factors. Table 5.21 contains the results of the factor analysis. Four factors were identified. Several things were considered when coming to this conclusion. There were three factors with eigenvalues greater than one, although the eigenvalue for factor four was very close to one (0.9899). Cattell's Scree Plot showed a large separation between factors 1 and 2, and a smaller separation between factors 4 and 5.

All three new risk factors were contained in a factor that was already represented by one of the five original risk factors. *Angina* was contained in factor 1, as was *four or more recorded diagnoses*. *Use of durable medical equipment* and *three or more hospitalizations in the previous year* were contained in factor 2, as was *six or more prescription medications*. Therefore, the three new risk factors did not represent any additional factors than what was already represented by the original five variables.

Based on these results, it was decided that the original regression model with the five risk factors was the optimal model for predicting PDRM. Although this model explained slightly less of the variance of PDRM than the second regression model with the seven risk factors, the original model is less complex and it contains variables that were hypothesized to be risk factors on either empirical findings or the conceptual framework used in this study.

Additional Analyses Related to Risk Factor Identification

Two additional analyses related to risk factor identification were performed. First, because it could be argued that one of the significant risk factors in the original model (*antihypertensive drug use*) may be in the model as a function of the operational definitions of

Table 5.21 Rotated (Varimax) Factor Matrix of Five Original Risk Factors and Three New Risk Factors

Variable	Factor 1	Factor 2	Factor 3	Factor 4
Angina	0.87			
Four or more recorded diagnoses	0.78			
Use of durable medical equipment		0.83		
Six or more prescription medications		0.57		
Three or more hospitalizations in the previous year		0.52		
Four or more prescribers			0.79	
Antihypertensive drug use			0.73	
Female gender				0.99
Eigenvalue	2.0059	1.0645	1.0155	0.9899

Only factor scores greater than +/- 0.40 are shown.

PDRM, an additional regression analysis was done, removing patients who had a PDRM with an antihypertensive drug specified in the operational definition from the analysis. This was performed to see if the model remained stable with the same risk factors, or if new risk factors would appear. Twenty-five patients were found to have a PDRM that contained an antihypertensive drug specified in the operational definition (representing PDRM #6, 15, 18, 37, 38, 42, 49, and 50). However, 20 of these 25 patients also experienced at least one other PDRM that did not contain an antihypertensive drug in the operational definition. Therefore, only five patients were removed from the analysis.

The results of this analysis can be seen in Table 5.22. The regression analysis included all 18 hypothesized risk factors. The resulting model contained all five risk factors from the original model: *four or more prescribers*, *four or more recorded diagnoses*, *female gender*, *antihypertensive drug use,* and *six or more prescription medications*. No new risk factors appeared in this new model. Therefore, because of the stability of the model, it was felt that the full model that includes *antihypertensive drug use* was acceptable.

A second additional analysis was performed to help delineate the relationship between *antihypertensive drug use* and *four or more prescribers*. This is because both of these risk factors fell into the same factor in the original factor analysis. Two regression models were performed taking either *antihypertensive drug use* or *four or more prescribers* out of the model and observing any change in the parameter estimate or odds ratio. When *antihypertensive drug use* was removed from the model, the parameter estimate and odds ratio for *four or more prescribers* remained fairly constant. In the original model, the parameter estimate was 0.2683 and the odds ratio was 1.308, while in this new model the parameter estimate was 0.3176 and the odds ratio was 1.374. When *four or more prescribers* was removed from the model, the parameter estimate and odds ratio for *antihypertensive drug use* did increase. In the original model, the parameter estimate was 0.7023 and the odds ratio was 2.018, while in this new model the parameter estimate was 1.0766 and the odds ratio was 2.935. Therefore, although the parameter estimate and odds ratio for *antihypertensive drug use* did increase, it did not account for the full effect of

Table 5.22 Logistic Regression Model Excluding *Antihypertensive Drug Use*

Variable	Parameter Estimate (b)	Standard Error (SE)	Chi Square Probability	Odds Ratio	95 Percent Confidence Interval
Four or more prescribers	0.2753	0.0612	0.0001	1.317	1.168-1.485
Four or more recorded diagnoses	1.0184	0.2546	0.0001	2.769	1.681-4.560
Female gender	-0.6824	0.2463	0.0056	0.505	0.312-0.819
Antihypertensive drug use	0.6183	0.2824	0.0286	1.856	1.067-3.228
Six or more prescription medications	0.6465	0.3050	0.0340	1.909	1.050-3.471
Equation Constant	-4.6792	0.2772	0.0001	-	-

four or more prescribers on PDRM. Thus, because of this, and the fact that these two variables are not highly correlated (0.2995), it was decided to include both variables in the final risk model. Overall, then, the original logistic regression model, which yielded five risk factors: *four or more prescribers*, *four or more recorded diagnoses*, *female gender*, *antihypertensive drug use*, and *six or more prescription medications* appears to be the most appropriate model for predicting PDRM.

Risk Stratification System

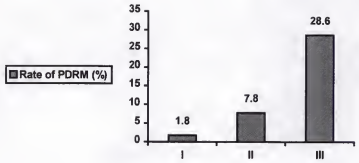
A risk stratification system was developed based on the five risk factors for PDRM. Patients were grouped into categories, based on the number of risk factors they had from the original regression model. Three categories were used: Stratum I, 0-1 risk factors; Stratum II, 2-3 risk factors; and Stratum III, 4-5 risk factors. The results of this risk stratification system can be seen in Figure 5.1. The Mantel-Haenszel Test was significant (chi square in 2 x 3 table = 63.81, $p<0.0001$), indicating that a definite trend was evident in the data; those patients who had more risk factors were associated with a greater risk of PDRM.

Testing the Hypotheses

Three sets of hypotheses were proposed and tested. The first set of hypotheses deals with the identification of risk factors for PDRM. The second hypothesis deals with general and drug (and disease) specific risk factors for PDRM. The third and final hypothesis deals with the relationship of PDRM to healthcare resource utilization. These three sets of hypotheses will be discussed in turn.

First Set of Hypotheses

The first set of hypotheses deals with the identification of major risk factors for PDRM in older persons.



PDRM pts	51	42	4
Total pts	2811	540	14

Risk Stratum
1 = 0 - 1 risk factors
2 = 2 - 3 risk factors
3 = 4 - 5 risk factors

Figure 5.1 Risk Stratification System

Hypothesis H1A

This hypothesis stated: "*Digoxin use* will be a risk factor for PDRM in older persons." While *digoxin use* was significantly associated with PDRM in the bivariate analysis (p value = 0.022), it was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1A is rejected.

Hypothesis H1B

This hypothesis stated: "*Antidepressant drug use* will be a risk factor for PDRM in older persons." While *antidepressant drug use* was significantly associated with PDRM in the bivariate analysis (p value = 0.002), it was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1B is rejected.

Hypothesis H1C

This hypothesis stated: "*Long-acting benzodiazepine use* will be a risk factor for PDRM in older persons." *Long-acting benzodiazepine use* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1C is rejected.

Hypothesis H1D

This hypothesis stated: "*Antihypertensive drug use* will be a risk factor for PDRM in older persons." *Antihypertensive drug use* was identified as a risk factor in the final prediction model for PDRM. Hypothesis H1D is supported.

Hypothesis H1E

This hypothesis stated: "*Gastrointestinal disorders* will be a risk factor for PDRM in older persons." While *gastrointestinal disorders* was significantly associated with PDRM in the bivariate analysis (p value = 0.001), it was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1E is rejected.

Hypothesis H1F

This hypothesis stated: "*Lung conditions* (lung disease, emphysema, bronchitis and asthma) will be a risk factor for PDRM in older persons." While *lung conditions* was significantly associated with PDRM in the bivariate analysis (p value = 0.019), it was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1F is rejected.

Hypothesis H1G

This hypothesis stated: "*Kidney disease* will be a risk factor for PDRM in older persons." While *kidney disease* was significantly associated with PDRM in the bivariate analysis (p value = 0.001), it was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1G is rejected.

Hypothesis H1H

This hypothesis stated: "*A history of falling* will be a risk factor for PDRM in older persons." *A history of falling* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1H is rejected.

Hypothesis H1I

This hypothesis stated: "*Four or more prescribers* will be a risk factor for PDRM in older persons." *Four or more prescribers* was identified as a risk factor in the final prediction model for PDRM. Hypothesis H1I is supported.

Hypothesis H1J

This hypothesis stated: "*Six or more prescription medications* in a drug regimen will be a risk factor for PDRM in older persons." *Six or more prescription medications* was identified as a risk factor in the final prediction model for PDRM. Hypothesis H1J is supported.

Hypothesis H1K

This hypothesis stated: "*Four or more recorded diagnoses* will be a risk factor for PDRM in older persons." *Four or more recorded diagnoses* was identified as a risk factor in the final prediction model for PDRM. Hypothesis H1K is supported.

Hypothesis H1L

This hypothesis stated: "*A previous adverse drug reaction* will be a risk factor for PDRM in older persons." *A previous adverse drug reaction* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1L is rejected.

Hypothesis H1M

This hypothesis stated: "*High alcohol consumption* will be a risk factor for PDRM in older persons." *High alcohol consumption* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1M is rejected.

Hypothesis H1N

This hypothesis stated: "*Self-assessment of poor health status* will be a risk factor for PDRM in older persons." While *self-assessment of poor health status* was significantly associated with PDRM in the bivariate analysis (p value = 0.001), it was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1N is rejected.

Hypothesis H1O

This hypothesis stated: "*Trouble paying for medications* will be a risk factor for PDRM in older persons." *Trouble paying for medications* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1O is rejected.

Hypothesis H1P

This hypothesis stated: "*Difficulty taking medications* will be a risk factor for PDRM in older persons." *Difficulty taking medications* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1P is rejected.

Hypothesis H1Q

This hypothesis stated: "*Patient belief that they are taking too many medications* will be a risk factor for PDRM in older persons." *Patient belief that they are taking too many medications* was not identified as a risk factor in the final prediction model for PDRM. Hypothesis H1Q is rejected.

Hypothesis H1R

This hypothesis stated: "*Female gender* will be a risk factor for PDRM in older persons." *Female gender* was identified as a risk factor in the final prediction model for PDRM, however, its odds ratio was less than 1, meaning that females are actually at less risk for a PDRM. Hypothesis H1R is rejected.

Second Hypothesis

The second hypothesis deals with the identification of general risk factors and disease or drug-specific risk factors for PDRM in older persons. This hypothesis stated, "there will be general and specific risk factors for PDRM in older persons."

The logistic regression analysis previously discussed was used as the basis to test this hypothesis. In the final logistic regression model, one drug-specific risk factor was identified (*antihypertensive drug use*), and four risk factors pertaining to general patient attributes related

to healthcare were identified: *four or more recorded diagnoses*, *male gender*, *four or more prescribers*, and *six or more prescription medications*. Hypothesis H2 is supported.

Third Hypothesis

The third hypothesis deals with the relationship of PDRM and healthcare resource utilization. This hypothesis stated, "Older persons that have PDRM will consume more health care resources than those who do not have PDRM." To test this hypothesis, each enrollee was classified as either having PDRM or not. Then, the utilization of health care resources was compared for the two groups. The results of this bivariate analysis can be seen in Table 5.23.

Patients with PDRM had statistically significantly more admissions to skilled nursing facilities, use of home health services, hospital admissions, emergency room visits, and use of one to two OTC medications. Patients with PDRM also had significantly more physician office visits and use of prescription medications in the higher end of these two categories (three or more visits, three to five medications, six or more medications). There was not a statistically significant difference between patients with, and without, PDRM in three areas of healthcare utilization: nursing home admissions, use of three to five OTC medications, and use of six or more OTC medications. The trend was in the direction of patients with PDRM for these three areas, though. Overall, then, patients with PDRM appear to use more healthcare resources then patients who do not have PDRM. Hypothesis H3 is supported.

Table 5.23 Bivariate Analysis of Patients With and Without PDRM, Categorized by Healthcare Resource Utilization

Healthcare Resource	No. (%) with PDRM (n=97)	No. (%) without PDRM (n=3268)	P value
Admission to a Skilled Nursing Facility	13 (13.4)	14 (0.4)	0.001[c]
Use of Home Health Services	6 (6.3)	49 (1.5)	0.001[c]
At Least One Hospital Admission	41 (42.3)	470 (14.4)	0.001[c]
At Least One Emergency Room Visit	40 (43.0)	550 (17.1)	0.001[c]
One to Two MD Office Visits	3 (3.2)	425 (13.2)	*0.001[c,d]
Three or More MD Office Visits	91 (95.8)	2644 (81.8)	0.001[c]
Nursing Home Admission	2 (2.1)	28 (0.9)	0.209[d]
One to Two Prescription Medications	28 (29.8)	1284 (40.0)	*0.047[a]
Three to Five Prescription Medications	40 (42.6)	969 (30.2)	0.010[b]
Six or More Prescription Medications	24 (25.5)	235 (7.3)	0.001[c]
One to Two OTC Medications	59 (62.1)	1490 (46.8)	0.003[b]
Three to Five OTC Medications	6 (6.3)	163 (5.1)	0.605
Six or More OTC Medications	1 (1.1)	14 (0.4)	0.357[d]

[a] Significance difference in variable between patients with, and without, PDRM, $p < 0.05$
[b] Significance difference in variable between patients with, and without, PDRM, $p < 0.01$
[c] Significance difference in variable between patients with, and without, PDRM, $p < 0.001$
[d] Probability value for Fisher's Exact Test
* Significance in opposite direction (Patients without PDRM were greater)

CHAPTER 6
DISCUSSION

This chapter will discuss the findings reported in the previous chapter. First, the Delphi technique and operational definitions of PDRM will be discussed. Second, the prediction models and risk factors for PDRM will be described in more detail. Third, the limitations, significance and implications of this research will be explored. Finally, some concluding remarks will be made.

Use of the Delphi Technique with the Geriatric Medicine Expert Panel

Drug-related morbidity is a widely recognized problem in older persons today. However, the phrase *preventable* drug-related morbidity has been far more controversial and less understood. When the term has been used in the medical literature, typically authors do not provide explicit definitions of what they mean. Others have different opinions of exactly which drug-related morbidities are preventable. This study represents the first attempt to develop explicit, operational definitions of PDRM.

Research question one asked what are the issues in developing operational definitions of PDRM with the Delphi technique. Several observations can be made about the usefulness of the Delphi technique with a panel of geriatric medicine experts to reach consensus on operational definitions of PDRM. This study showed it is possible to promote convergence of opinion on PDRM. Consensus was reached after only two rounds and opinion did not widely vary between the two rounds. Goodman (1987) states that it is the stability of the group response to an item

between the rounds which is important in the Delphi technique. There is some evidence that the comments written by other panel members in round 1 did influence the opinion of the panel members. There was only one written comment that indicated the group opinion had moved the panel member to change his opinion against his will: "I'll go with the group, but this is generally not the practice." Other than this sole comment, there was no evidence of "groupthink." Other written comments indicate that some members with strong opinions on certain types of PDRMs were not willing to change their opinion, e.g.: "Still stick with my original comments despite being in the minority." Overall, however, the process did promote consensus, which is one of the chief advantages of the Delphi technique (Delbecq, de Ven and Gustafson, 1986).

Using the Delphi technique also provided insight into the decision-making process that the panel members used. The comments made by the panel members suggest that they did take into account all four of the defining characteristics of PDRM. The first defining characteristic of a PDRM is whether health professionals should recognize significant problems in this pattern of care. There were not many comments related to this question, as one might expect. The patterns of care were included in the survey with the belief that there was a problem with them, and the panel members were asked to make comments only if they did not agree there was a significant problem in the pattern of care. Still, some comments indicated that the panel members believed the problem in the pattern of care may not have been that great. For example, one panel member suggested that failure to give cytoprotective agents (the pattern of care) would be not be inappropriate: "But cytoprotective agents may not prevent the adverse outcome."

The second question the panel members were requested to consider was whether health professionals should foresee the possibility of the outcome. Some panel members commented that the outcome was so infrequent they may not foresee the possibility of it occurring: "Very uncommon" and "Very rare in healthy patient."

The third question the panel members were asked pertained to identifying the cause of the outcome. This defining characteristic of a PDRM seemed to generate the most comments. The majority of these comments indicated that for certain clinical scenarios, they were unable to distinguish the real cause, due to the complexity of the scenario: "depends on other drugs in use," "Concomitant hypertension? Concomitant diuretics?," and "Too many other factors usually involved." Some of the comments stated that the cause-effect relationship, as outlined in the pattern of care and outcome presented, was not clear enough: "the role of NSAIDs may be minor," and "Beta blockers not uniformally or clearly significantly associated with depression."

The final question the panelists were requested to consider asked if the cause of the outcome was controllable. There were a few comments related to this question. These comments addressed the issue that often the pattern of care which lead to the outcome is necessary (risk versus benefit) or the outcome may still occur even if the pattern of care were changed: "Still feel that can occur no matter how diligent the care."

Therefore, in answer to research question one, it appears that the Delphi technique was useful and successful in obtaining consensus on operational definitions of PDRM.

Two other issues that merit discussion are the characteristics of those clinical scenarios that were rejected and those that were added by the expert panel. Six clinical scenarios were rejected by the expert panel. All four defining characteristics of a PDRM seem to have been influential in the panel's decision to reject these clinical scenarios. For example, one panel member did not *recognize* a problem with failure to monitor theophylline because, "theophylline isn't potent enough to prevent exacerbation [of asthma]." The group consensus on rejecting acute renal failure due to poor allopurinol monitoring is that they would not *foresee* the possibility of the outcome because it is so rare. One panel member rejected digoxin toxicity with inappropriate digoxin monitoring as a PDRM because that member felt the cause of the toxicity could not be *identifiable* - the patient may be on other medications that interact with digoxin. Finally, falls

due to use of antiparkinsonian agents appears to have been rejected by the panel because (1) the cause of the falls could not *identifiable* (both the drugs and the disease itself cause falls) and, (2) the panel could not *change* the pattern of care (people with Parkinson's disease need to be on these drugs, even though they cause falls, because there are no alternatives).

The additional types of PDRM proposed by the expert panel represent a wide array of clinical conditions and outcomes. Only three of the proposed types would not have met the initial inclusion criteria; they represented relatively minor clinical outcomes (one outcome was rebound congestion and two were acute urinary retention). The initial list of clinical scenarios in older persons was not intended to be an all-inclusive list of PDRM, so the fact that so many additional clinical scenarios were suggested by the expert panel (who work in a wide variety of clinical settings) should not be too surprising.

The creation of these operational definitions of PDRM is an important first step - but it is just that - a first step. Over time, these definitions will need to be updated and revised as clinical practice and standards of care progress. As well, this exercise was limited to only PDRM in older persons. It would also be useful to replicate this study with a different panel of geriatric medicine experts and to compare the results. Finally, the creation of operational definitions on PDRM in older persons may help to establish new standards of care in geriatric medicine.

Consensus-Approved Operational Definitions of PDRM Observed in the Study Population

A wide variety of outcomes that matched the consensus-approved operational definitions of PDRM were identified in the study population. As stated in the results section, 1005 such outcomes were identified. The outcome that occurred with the greatest frequency was the outcome for PDRM 16 (congestive heart failure and/or heart block: see Appendix G). However, this outcome occurred in only 46 patients, or 4.6 percent of all outcomes. There were seven

outcomes associated with operational definitions of PDRM that were not found at all in the study population.

While a wide variety of outcomes were found in the study population, a few specific operational definitions of PDRM were responsible for a large percentage of total PDRMs found. The most frequently occurring operational definition of PDRM was found 24 times (15.2 percent of all PDRMs): secondary myocardial infarction without ASA and/or beta-blocker use. The second most frequently occurring operational definition of PDRM was found 18 times (11.4 percent of all PDRMs): hospitalization due to hypogylcemia for those patients taking an oral hypogylcemic without regular hemoglobin A1c monitoring. Overall, the top five operational definitions of PDRM were responsible for almost half of all PDRMs found (46.8 percent). There were 23 consensus-approved operational definitions of PDRMs that did not occur even once in the study population. It appears that just as a small proportion of patients and diseases are responsible for a large proportion of healthcare costs, a small proportion of PDRMs are responsible for most PDRMs.

As presented in the last chapter, 11 out of the 52 consensus-approved operational definitions of PDRM were suggested by the Geriatric Medicine Expert Panel after the first round of the Delphi technique. These 11 additional operational definitions of PDRM occurred less frequently than the other 41 types of PDRM. Although the 11 operational definitions accounted for 21.2 percent of all 52 operational definitions of PDRM, they only accounted for 16 (10.1 percent) out of all 97 PDRMs identified in the database. Only one of these 11 additional operational definitions of PDRM occurred in more than three patients (acute urinary retention in patients with a history/diagnosis of benign prostatic hypertropy with use of an anticholingeric agent). Therefore, while the large number of additional PDRMs proposed and accepted by the Geriatric Medicine Expert Panel suggests that there are many additional PDRMs in older persons other than the initial list, the initial list may represent the most frequently occurring operational

definitions of PDRM. One of the inclusion criteria for a clinical scenario being on the initial list was that it occurs commonly in older persons.

A majority (62.9 percent) of the patients who had PDRM experienced only a single specific operational definition of PDRM. Still, a considerable percentage (37.1 percent) of patients with PDRM experienced more than one specific operational definition. Almost nineteen percent (18.6 percent) of patients with PDRM experienced three or more specific operational definitions of PDRM. One patient experienced five specific operational definitions of PDRM.

Many of these patients who experienced more than one PDRM had PDRMs which shared the same outcome. For example, one patient had an emergency room visit/hospitalization due to congestive heart failure (the outcome), but met the pattern of care for three specific operational definitions of PDRMs related to this outcome (#16, 42, and 43). Overall, 28 (28.9 percent) out of 97 patients with PDRM had multiple operational definitions of PDRM that shared the same outcome. This finding should not be too surprising. First, the operational definitions of PDRM were not designed to be mutually exclusive. That is, patients may have two or more inappropriate patterns of care that led to the same outcome. Several of the operational definitions of PDRM contain the same outcome. For example, emergency room visit/hospitalization due to a major or minor hemorrhagic event is the outcome in four specific operational definitions of PDRM. Second, there is some empirical evidence that patients who experience an adverse drug event are at higher risk for a second adverse drug event (Hurwitz, 1969; Zilleruelo, Espinoza and Ruiz, 1987), therefore the same could be true for PDRM. For this reason, a past history of an adverse drug reaction was included in the list of hypothesized risk factors for PDRM in this study. Third, some patients may suffer from general medical mismanagement. Their medical care may be lacking in one or more of the eight necessities of the medication use process (Grainger-Rousseau et al., 1997). For example, if the patient has multiple prescribers who are not communicating their therapeutic plans to one another, the patient may be taking a dangerous

combination of medications, placing that patient at greater risk for a PDRM. This could be the cause of the problem for the patient identified with three inappropriate patterns of care related to congestive heart failure, where all three patterns may have contributed to the outcome.

Validation of Operational Definitions of Preventable Drug-Related Morbidity

This study showed that classification of PDRM, based on operational definitions of PDRM, is valid as compared to the clinical judgements of a panel of pharmacists. The overall sensitivity of 87.5 percent and specificity of 73.5 percent for both operational definitions of PDRM tested actually exceeded the initial target sensitivity and specificity. These results are encouraging for several reasons. First, the high specificity indicates that most people who do not have PDRM are correctly classified as such by the operational definitions. Although the implementation of these definitions in patient care is beyond the scope of this study, if they were used clinically, the high specificity will prevent a lot of unnecessary work. Pharmacists and other health care professionals can be fairly certain that patients identified by the definitions as having PDRM, will be found to have PDRM upon review. Second, the sensitivity is high enough to correctly identify over 87 percent of patients who actually have PDRM. This finding suggests that more of the study population has PDRM than the 2.9 percent identified by the operational definitions. This would be more consistent with other estimates of the incidence of PDRM (Lazarou et al., 1998). This finding, along with the fact that there may be other operational definitions of PDRM approved by other panels, further emphasizes that this 2.9 percent is really a lower-bound estimate of the incidence of PDRM. Further investigations may focus on refining the definitions in an attempt to identify more patients with PDRM.

As was mentioned in the results section, the chart abstracts for the patients with the hyperglycemia outcome had to be re-administered to the Patient Chart Abstract Panel. This is

because the pharmacists did not appear to follow the specific operational definition, but instead looked for other cases of PDRM related to the outcome (hyperglycemia) in these patients. This conclusion was made based on verbal and written comments by the panel members.

There are two factors that might help to explain why the pharmacists deviated from the operational definition in the first validation exercise for the hyperglycemia outcome. First, several patients who did not meet this operational definition for a PDRM (outcome = hypergylcemia with pattern of care = patient on an oral hypoglycemic with no regular HgA1c monitoring) did meet the operational definition for another PDRM with the same outcome. This overlapping definition of PDRM is outcome = hyperglycemia or hypogylcemia with pattern of care = use of insulin and no regular HgAlc monitoring (see #51 in Appendix G). Therefore, it was very possible that the pharmacists felt that although the patient did not meet the first operational definition of PDRM, since the patient was also on insulin, and it was related to the same outcome (hypergylcemia), they classified the patient as having PDRM. In future investigations, the operational definitions of PDRM that do not overlap in the "outcome" with other operational definitions should be chosen when testing sensitivity and specificity (such as the PDRM related to secondary myocardial infarction). A second factor to explain the differences between the pharmacist and operational definition classification could be the pharmacists' clinical judgement. Many of the patients classified as having PDRM by the pharmacists were not on insulin or an oral hypoglycemic. Hemoglobin A1c monitoring is not typically done on diabetes with mild disease, which these patients probably had. Still, most panel members felt they should have regular HgA1c monitoring. This could mean either the pharmacists did not completely understand the questions related to PDRM or they were lacking in their medical knowledge. The pharmacists on this panel were not chosen for their expertise in diabetes so a possible future investigation could involve repeating this exercise with experts in the care of diabetics (diabetic educators, etc.). Upon re-administration of the chart abstracts,

however, pharmacist agreement with the operational definition was very high so this second factor seems unlikely.

Many of the discrepancies between the pharmacists' and operational definition classification of patients with the secondary myocardial infarction outcome seem to be related to details in patient care that the operational definition does not address. The pharmacists listed many reasons why they felt patients should not be on either ASA or a beta-blocker in specific situations. For ASA, reasons the pharmacists felt the patient should not be on it (and therefore it would not be a case of PDRM) include: the patient was on warfarin (drug interaction), aspirin allergy, documented nose bleeds with high-dose ASA, history of gastrointestinal bleeding, patient was on ibuprofen and naproxen (drug interaction), and patient had peptic ulcer disease. The panel members also listed several reasons why the risk of being on a beta-blocker would outweigh benefits of preventing a secondary myocardial infarction: patient had second degree heart block, sinus bradycardia, right bundle branch block, hyperlipidemia, congestive heart failure, peripheral vascular disease, and patient was taking diltiazem (combined negative intropic effects with a beta-blocker). Several pharmacists noted that although the patient was on a beta-blocker, the dosage was too low and therefore even though the operational definition did not classify it as a PDRM, they felt it was a PDRM. One pharmacist noted that the patient's previous myocardial infarction was over five years ago, thus that pharmacist felt the patient did not need to be on preventive medicine (beta-blocker or ASA).

Risk Factors for PDRM

Phase II of this study involved identifying risk factors for PDRM in older persons. Five risk factors for PDRM were identified in the final prediction model. Each of these risk factors will be discussed in turn.

Risk Factor 1: *Four or More Recorded Diagnoses*

Four or more recorded diagnoses was one of the 18 hypothesized risk factors that was a significant risk factor for PDRM in the final prediction model. As was discussed in chapter three, this variable was included for empirical reasons (Carbonin et al., 1991; O'Neil and Poirer, 1998) and because patients with multiple diseases often receive care from multiple physicians, who may have differing or conflicting therapeutic plans due to poor communication, which may result in PDRM.

Risk Factor 2: *Antihypertensive Drug Use*

Antihypertensive drug use was also one of the 18 hypothesized risk factors that was a significant risk factor for PDRM in the final prediction model. *Antihypertensive drug use* was included for empirical (Larson et al., 1987; Williamson and Chopin, 1980) and theoretical reasons. It was felt that because of the numerous side effects, drug interactions, and contraindications with the use of antihypertensive medications, proper therapeutic monitoring (one of the eight essential elements of drug use) is very important.

It could be argued that *antihypertensive drug use* is a risk factor because it is contained in the some of the operational definitions of PDRM. This does not appear to be the case, as when patients who experienced a PDRM with an antihypertensive drug in the operational definition were removed from the analysis, *antihypertensive drug use* remained in the prediction model. While some of the PDRMs did include antihypertensive drugs in the operational definition, the inappropriate pattern of care for the top kind of PDRM identified (secondary myocardial infarction with no ASA and/or beta-blocker use) actually specifies that beta-blockers (an antihypertensive) were *not* used.

Risk Factor 3: *Male Gender*

Female gender was one of the 18 hypothesized risk factors for PDRM. However, while *female gender* was identified in the final prediction model, the odds ratio was less than one, meaning that *male gender* was the actual risk factor. This result is opposite the hypothesized relationship, but it may not be too surprising. It was acknowledged in chapter three that the empirical evidence of *female gender* being a risk factor was mixed, and, in fact, some authors argue that by excluding pregnancy and female-specific drugs, females are not at a higher risk (Zadoroznyj and Svarstad, 1990). In this population of older persons, pregnancy is obviously not a consideration. As well, a review of the final 52 types of PDRM reveals that there are no female-specific types of PDRM listed, while there are some types of PDRM that are either exclusive to males (acute urinary retention for patients with benign prostatic hypertropy and the use of anticholingeric agents), or either occur predominantly in males (secondary myocardial infaction without the use of ASA and/or a beta-blocker). There is some evidence in the literature that males adhere less to medical instructions than females, which may also lead to PDRM (Oldenburg, MacDonald and Perkins, 1988). Finally, it was acknowledged in chapter three that *female gender* did not seem to fit within the conceptual framework (medication use system and biopsychosocial model).

Risk Factor 4: *Four or More Prescribers*

Four or more prescribers was one of the 18 hypothesized risk factors that was a significant risk factor for PDRM in the final prediction model. It was included as a possible risk factor mainly based on theoretical considerations. Theoretically, if a patient has multiple prescribers, PDRM could develop from competing prescribing objectives, and poor documentation and communication of information and therapy decisions.

Risk Factor 5: *Six or More Prescription Medications*

Six or more prescription medications was also one of the 18 hypothesized risk factors that was a significant risk factor for PDRM in the final prediction model. It was included as a possible risk factor mainly based on empirical considerations. As was discussed in chapter three, there is considerable empirical evidence in the medical literature that the risk of drug-related morbidity increases with an increase in the number of medications in the drug regimen. (Hurwitz, 1969; Braverman et al., 1996; Carbonin et al., 1991; Fouts et al., 1997; Larson et al., 1987).

General Discussion on the Final Prediction Model for PDRM

The final prediction model for PDRM merits discussion. The final model consisted of five risk factors, four of which were hypothesized to be risk factors and one that had a relationship opposite to the hypothesized direction (gender). This model demonstrates that a wide variety of factors influence PDRM, not just drugs themselves or certain diseases. This supports the idea that the medication use system is influenced by numerous factors. In fact, only one of the five risk factors is a drug class (*antihypertensive drug use*). This also supports the use of the biopsychosocial model, which says health outcomes are not just related to a patient's physiological status (Engel, 1977). The final prediction model contains risk factors that include things other than just drugs and measures of health status.

There may be some surprise that so few of the initial 18 hypothesized risk factors ended up in the final prediction model. Although there was both empirical and theoretical evidence for making hypotheses about all 18 risk factors, few studies have included all these variables (and the 27 additional variables) in one prediction model. In the past, most authors have considered only a few variables in each study. Therefore, the amount of variance explained for PDRM in the literature would exceed 100 percent if each risk factor explained independent proportions of variance. It was clear that not all of the 18 hypothesized risk factors would end up in the final

model. Future investigations may focus on still more possible risk factors for PDRM that were not included in this investigation.

Although the factor analysis did not yield factors that related to definite constructs, and therefore an analysis incorporating factor scores was not used, the factor analysis still yielded some noteworthy results. First, some of the factors do appear to relate to constructs within the medication use system and biopsychosocial model. Factor 1, which contained *kidney disease*, *gastrointestinal disorders*, *four or more recorded diagnoses*, and *lung conditions*, may to relate to the patient's disease. Factor 2, which contained *four or more prescribers*, *antihypertensive drug use*, and *antidepressant drug use*, may relate to long-term prescriptions, although this was not clear. Factor 3, which contained *six or more prescription medications*, *digoxin use*, and *self-assessment of poor health status*, was difficult to relate to one particular construct. Some possibilities are illness, frailty, poor monitoring, or drug interactions. Factor 4, which contained *a history of falling*, *difficulty taking drugs*, and *long-acting benzodiazepine use*, may relate to cognitive difficulties/impairment. Factor 5, which contained *a patient belief that they are taking too many medications*, *trouble paying for medications*, and a *previous adverse drug reaction*, may relate to the patient's attitude toward medications. Finally, factor 6, which contained *high alcohol consumption* and *female gender*, may relate to female gender.

The factor analysis also failed to show an exact relationship to the proposed underlying structure for this study (see Table 4.3). Although some possible similarities may be observed between the factors identified and the proposed structure, overall there were many differences. This result should not be too surprising. The proposed structure contained constructs whose relationships have been relatively untested to date. The factor analysis performed in this study may help guide future research in determining the nature of these relationships.

In the factor analysis, two of the final five risk factors were contained in factor 2 (*antihypertensive drug use* and *four or more prescribers*). Both factors were left in the final prediction model based on the their relatively low correlation, stability of their odds ratios and parameter estimates when one of them was removed from the regression models (see previous

chapter), and the inability to definitely assign a construct to factor 2. The risk stratification system developed in this study treated them as separate risks, with the acknowledgement that further research may prove that they really do represent the same construct.

The application of the prediction model for PDRM is beyond the scope of this study, but some general principles may still be stated. As was discussed in chapter two, the risk factors in this study are those variables that are statistically associated with PDRM (the outcome event) in older persons. They represent patient characteristics, mainly healthcare demographics. Some of the patient characteristics, or risk factors, can not be easily changed, such as gender, while others can be modified (e.g.; by reducing the number of prescribers for a given patient). Using the risk stratification system developed in this study, patients with multiple risk factors for PDRM could be identified by health plans or individual physicians and then proactively managed to help prevent PDRM and allocate resources in the most efficient manner. The types of patient management will be varied, but regardless, the interventions should be based on how the risk factors relate to the key constructs in the medication use system and the biopsychosocial model. For example, we know that physician-pharmacist-patient communication is a necessity of the drug use system, and therefore if a patient has *four or more prescribers*, attempts should be made to improve communication by reducing the number of prescribers or better coordination of therapy. Other researchers in the future may investigate whether the risk factors identified are truly causal or predictive and they may attempt to see how these risk factors relate to other healthcare models and theories. For example, as discussed, further research may be conducted to determine the causal relations that may underlie the identification of *antihypertensive drug use* as a risk factor.

General and Specific Risk Factors

Both the specific and general risk factors are a function of the operational definitions used to identify patients with PDRM. As was previously discussed, *antihypertensive drug use* is

contained within some of the operational definitions of PDRM. The general risk factors identified are only general in the sense that they are risk factors for the 52 types of PDRM approved by the expert panel. However, there can be some confidence that these represent the main types of PDRM since (1) round 1 of the survey contained PDRMs believed to be common and serious, (2) the panel members had the opportunity to add additional PDRMs, and (3) a small percentage of the 52 operational definitions of PDRMs were responsible for the majority of the PDRMs identified in the study population. Therefore, the general risk factors identified may be general risk factors for PDRM in older persons, not just for these 52 operational definitions. Still, further research will be needed to determine whether these general risk factors remain the same in other patient populations (pediatrics, younger adults, etc.) and settings (other than Medicare managed care plans).

PDRM and Healthcare Resource Utilization

As was hypothesized, patients with PDRM use significantly more healthcare resources than those patients without PDRM. This relationship does not imply causality, however. For example, while patients with PDRM had more hospitalizations and emergency room visits, perhaps being in those settings places people at greater risk for PDRM. However, the idea that PDRM increases resource utilization is supported by the literature reviewed in chapters one and three. There have been many estimates of the additional costs incurred to the healthcare system by improper drug therapy management and drug-related morbidity and mortality (Johnson and Bootman, 1995; Bates et al., 1997).

Potential Limitations

Some potential limitations of this study relate to the creation and validation of the operational definitions of PDRM. Although the method for selecting PDRMs has been described,

perhaps another panel would select different operational definitions of PDRM. As well, this study defined only a subset of PDRM. The operational definitions of PDRM that were developed will require testing in other settings and populations. As previously mentioned, a potential limitation of this study is the lack of an accepted "gold standard" to determine what is, and is not, PDRM. In this study, the Chart Abstract Reviewer Panel of five pharmacists was used. Although their judgements were influenced by the presentation of the patient in the chart abstract and their own biases, it was felt that this was the best validity check available for the operational definitions of PDRM.

Some potential limitations pertain to the identification of risk factors for PDRM. Only risk factors associated with PDRM in older persons were considered. Risk factors may differ for other populations and it may differ for PDRMs in older persons that were not investigated in this study. Patterns related to definite constructs for risk factor groupings could not be recognized from the factor analysis. While the list of possible risk factors considered in this study was more thorough than any other study in the peer-reviewed medical literature, there could potentially be additional risk factors that may contribute to the regression models. Some potential risk factors for PDRM, such as an abnormal potassium level, drug interactions, and a patient belief that the drugs were responsible for hospitalization, have been previously shown to be risk factors for adverse drug events, but could not be tested in this study due to limitations of the study database. For example, although the study database listed all laboratory tests performed on any given patient, it did not contain the actual value of the test.

Finally, there are some potential limitations with the study population used in this study. The study population was limited to those individuals enrolled in the Florida Hospital Healthcare System Premier Plan and who completed the PWP Senior Assessment tool. Since enrollment in the plan was optional, the study population may not be totally representative of the older population in general. As well, those older persons who elected to complete the PWPs may be

different from those who did not complete the instrument. However, a previous study of Medicare beneficiaries concluded that older persons who participate in screening services (such as completing a risk assessment questionnaire) did not differ significantly in their health behaviors from older persons not participating in the preventive services (Schweitzer et al., 1994). A study that included 217 noninstitutionalized older persons in Sweden also concluded that those older persons who do, and do not, participate in health promotion activities do not differ in health status (Augustsson et al., 1994). Older persons enrolled in a managed care Medicare-risk health plan may differ demographically and may have different health care resource utilization and outcomes that those older persons not in these plans. One study that compared older persons with joint or chest pain in traditional Medicare and Medicare-risk health plans found little significant difference, although the patients in the managed care environment had reduced utilization of services and poorer improvement of symptoms in one of four outcomes considered (Clement et al., 1994). In contrast, another study which compared ten HMOs with Medicare risk contracts to ten traditional fee-for-service plans found that enrollment status was not significantly associated with functional status or medical visits (Retchin et al., 1992).

Significance

Healthcare administrators who are interested in reducing healthcare costs should be particularly interested in the relationship between healthcare resource utilization and PDRM, and the risk stratification system developed in this study. The prediction model and risk stratification system developed may allow identification of high-risk patients and potential high utilizers of valuable health care resources, thus contributing to an efficient allocation of scarce "preventive" resources. This would concur with Anderson and Knickman's (1984) argument that focused

attention must be placed on older persons who are high utilizers of medical services. McCall and Wai (1983) also argue for the study of patterns of utilization in older persons and add that strategies targeted to high cost enrollees have the potential for a strong impact on resource utilization. Boult et al. (1995) claim that the first step of any geriatric evaluation and management program is the identification of high risk. Others have argued that risk identification, and proposing interventions based on those risks, are essential elements to increase the span of healthy life in older persons (Collier, Kinion and Brodbeck, 1996). Johnson and Bootman (1995) state that older persons are at particular risk for drug-related problems, which can lead to PDRM. Plushner and Helling (1996) argue that studies should be performed in the future to identify risk factors for PDRM in older persons. That was the intent of this study. Pharmacy managers and administrators may be able to use the results of this study to reallocate resources in the most effective and efficient way possible.

The identification of the significant risk factors for PDRM should support the development of a rational basis for planning and implementing interventions to reduce drug-related morbidity and mortality in older persons. Hopefully, this system will allow the identification of individuals who have the greatest need of pharmaceutical care. Future studies may be able to use this knowledge to perform pharmaceutical care interventions that will have the potential to deliver the greatest good, and test the results of these "targeting" pharmaceutical care interventions. Pharmacists working in settings other than hospitals and nursing homes will especially benefit from this study, as PDRM has been inadequately studied in the community setting (French, 1996). Fincham (1996) argues that meeting the health care needs of older persons will involve restructuring health care delivery and an essential component of this restructuring will include preventing adverse drug-related episodes. He adds that pharmacists must take a more active role in decreasing therapeutic failure and the occurrence of PDRM and one way of doing this is the proactive avoidance of adverse drug effects (Fincham, 1996).

Finally, healthcare administrators in captitated Medicare plans may be particularly interested in the relationship of PDRM to resource utilization and the risk stratification system. Here, need for adequate identification of high-risk patients is essential. An additional challenge is the management of pharmacy benefits within these types of plans (Nee and Schwab, 1997). It is hoped that this project may allow for better management of the pharmacy benefit and the total health care benefit in general. The ability to target certain individuals at risk for PDRM may be a valuable tool for health care clinicians and administrators.

Overall, then, if PDRM in older persons is to be decreased, operational definitions of PDRM are needed and those older persons who are at high risk must be identified prospectively. It is hoped by addressing these important issues, this study will add significantly to the medical literature and to medical practice.

Contribution to the Profession of Pharmacy

While many authors have agreed that PDRM is an important problem and the resolution of this problem fits into the mandate of the profession of pharmacy, there is a lack of agreement as how to best approach this issue. Hopefully this study will give pharmacists the tools they need to identify which individuals should receive additional monitoring.

Contribution to Healthcare

Numerous healthcare organizations have argued for more research in the area of geriatric medicine and, in particular, for PDRM. One of the areas recommended for more research by the Institute of Medicine's Committee to Develop an Agenda for Health Outcomes Research for Elderly People was how different treatments, including drugs, affect older individuals' health outcomes (Feasley, 1996). Identifying and preventing drug-related morbidity in older persons is

one goal of Healthy People 2000 (U.S. Department of Health and Human Services, 1991). Finally, "When Medicine Hurts Instead of Helps", a recent report by the Alliance for Aging Research, recommended that more research be done to determine which older persons are at risk for medication-related problems (Alliance for Aging Research, 1998).

This study will hopefully help these organizations and healthcare professionals through the creation of operational definitions of PDRM and potential indicators for PDRM.

Theoretical Contribution

This study has created operational definitions of PDRM in older persons. This is currently lacking in healthcare. There is no consensus about exactly which drug-related problems would have the characteristics of being recognizable, foreseeable, identifiable, and controllable, and few authors have explicitly described the standard that they used in judging events as preventable. Ultimately, judgements of preventability may depend on the development of consensus standards for medication use. By developing explicit operational definitions and testing their association to other elements of care, this research project will promote further research and advance the development of improved standards. Such definitions will not only help to distinguish preventable from nonpreventable drug-related morbidity and mortality, but should foster more research in this area by providing others with readily available definitions to use in other research studies. This research could be in the form of program evaluation or testing "targeting' pharmaceutical care interventions.

Conclusions

This study, *risk assessment of preventable drug related morbidity in older persons*, had three initial research objectives. The first research objective was to create operational definitions of preventable drug-related morbidity (PDRM) in older persons. This research objective was accomplished through using the Delphi technique with a geriatric medicine expert panel to create 52 operational definitions of PDRM in older persons. These operational definitions were then validated through the use of a chart abstract reviewer panel. This is the contribution to methodology of this research, since such a consensus on the operationalization of PDRM was previously lacking in the medical literature.

The second research objective was to identify patients who are at particular risk of PDRM and who may therefore benefit from comprehensive pharmaceutical care. Here, a prediction model was created to identify risk factors for PDRM. Eighteen initial hypothesized variables were proposed based on empirical findings and the medication use system and biopsychosocial model. The dependent variable was the existence of PDRM (as defined) and the independent variables were the hypothesized risk factors. Factor analysis and logistic regression models were used to identify risk factors for PDRM. Five risk factors for PDRM were identified in the final prediction model: *four or more prescribers*, *four or more recorded diagnoses*, *antihypertensive drug use*, *male gender*, and *six or more prescription medications*.

The third research objective was to create a risk stratification system for PDRM. A risk stratification system of three categories was developed for PDRM based on the number of risk factors present in an individual patient. This system will hopefully aid health care professionals to determine the risk of PDRM in an individual patient, based on how many of the five risk factors are present in that patient.

While it was not a primary research objective, patients with PDRM were shown to use significantly more healthcare resources then patients who did not experience a PDRM in many key areas.

The outcome of this research project will ultimately be measured by two things. First, the results of this study will either be confirmed or rejected by subsequent studies in the future. Other studies will need to be conducted to answer some of the new questions raised by this study. This includes determining what are the risk factors for PDRM in other settings and patient populations. Second, the outcome of this study will also be determined by the incorporation of the study results into actual patient care. It is intended that the prediction model and risk stratification system developed in this study will help pharmacists and other healthcare professionals by providing them a tool for the identification of older persons who may be at particular risk of PDRM. For example, knowing that patients taking antihypertensives are at a two-fold increased risk of developing a PDRM will be valuable information for physicians, pharmacists, and other health care professionals. It is hoped that implementation of the prediction model created in this study will help prevent patients from developing PDRM in the future.

APPENDIX A
GERIATRIC MEDICINE EXPERT PANEL MEMBERS

Expert Panel Member	Title	Additional qualifications in geriatric medicine
Lee Adler, DO	Medical Director, FHHS	
John Fleming, MD	Assistant Director of Internal Medicine Florida Hospital Family Practice Residency	Board certified in Geriatrics
Paul Garrett, MD	Senior Medical Director, Florida Hospital Healthcare System	
Manoucher Manoucheri, MD	Associate Director of Internal Medicine Florida Hospital Family Practice Residency	
Gary Miller, MD	Medical Director of several long-term care facilities	Board certified in family practice & geriatrics
Hang Nguyen, Pharm.D.	Clinical pharmacist, Premier Care Plan	
David Pocock, MD, MBBS	Internal Medicine Physician	Board certified in geriatrics

APPENDIX B
EXAMPLE SURVEY FOR GERIATRIC MEDICINE EXPERT PANEL MEMBERS – ROUND 1 OF DELPHI TECHNIQUE

July 24, 1998

Dear <Geriatric Medicine Expert Panel Member>,

Congratulations on being appointed a member of the Geriatric Medicine Expert Panel by Dr. Paul Garrett! As you know, a major problem in the health of older persons is *preventable* drug-related morbidity. Your expertise will be used to determine whether the following drug-related morbidities in older persons are **recognizable, foreseeable,** and if **causality** can be **identified and controlled**.

Please see the following **Survey Instructions** for details on how you can help to define preventable drug-related morbidities in older persons. Based on the experience of others, it will take approximately 20 minutes to complete the survey.

Your input is important, as there are only seven members of the Geriatric Medicine Expert Panel. Please return the list of possible preventable drug-related morbidities with your comments by **Friday, July 31, 1998** to ensure that your input is considered. Approximately one week after that, you will receive a revised version of the survey, based on the comments of all panel members. Please do not distribute or reproduce this survey without permission.

You can fax the survey back at (352) 392-7782. Feel free to call with any questions at (352) 846-0163 or use the following e-mail address:neil@cop3.health.ufl.edu. Again, thank you.

Sincerely, Neil M[ac]Kinnon, M.S., R.Ph.

Survey Instructions

You will be helping to define *preventable drug-related morbidities* in older persons. First, here are a couple definitions:

(1) A drug-related morbidity (adverse drug event, drug misadventure) is defined as a clinical outcome in which drug therapy has not produced a reasonable intended result either by (a) producing a noxious, unintended and undesired drug effect, or (b) by failing to produce the intended effect within a reasonable time.

(2) A ***preventable*** *drug-related morbidity* (a) results from unacceptable quality of care (e.g., failure to meet consensus guidelines) or (b) occurs after a *drug-related problem*. There are four defining characteristics of a preventable drug-related morbidity. The *drug-related problem* must be recognizable and the likelihood of a drug-related morbidity must be foreseeable. In addition, the cause(s) of the problem (and subsequent drug-related morbidity) must be identifiable, and those causes must be controllable. *Preventable drug-related morbidity*, therefore, results from unrecognized or unresolved *drug-related problems*.

● A *drug-related problem* might be recognizable and interpretable by the patient in whom the event occurs, a lay caretaker, or a health professional (physician, pharmacist, etc.).

Here are the survey instructions:

● The **objective of this exercise**, given a specific *drug-related morbidity*, is to develop criteria for the four defining characteristics. Each of the following examples will describe a *drug-related morbidity* and additional information that may or may not (in your judgement) relate to quality standards or describe a drug-related problem.

● In order to evaluate whether the following examples are types of preventable drug-related morbidities, you should read the **outcomes** and **patterns of care** and answer the following questions:

1. *For most older persons, should health professionals (MDs, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care?*
2. *For most older persons, should health professionals be able to **foresee the possibility of the outcome,** if those problems were not resolved?*
3. *Should most health professionals **see how to change** the pattern of care to prevent the outcome?*
4. *Should most health professionals **actually change** the pattern of care?*

● If you answer "**Yes**" to all four of these questions, then this is a type of preventable drug-related morbidity and you should check the "**Yes**" box.

● If you answer "**No**" to one or more of these questions, then this is **not** a type of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why. You may wish to describe whether there is some other element that could be added to the pattern of care that would make it a stronger, clearer or less ambiguous definition of preventable drug-related morbidity. This section is very important to complete. Please be as specific as you possibly can. For example, if you believe the pattern of care should be changed (e.g. a lab value should be monitored every 2 months instead of every 3 months) or something is

missing (e.g.; a duration of use of a drug should be specified) then please write that in the space provided. Also, if you felt the possible preventable drug-related morbidity did not meet any one of the four criteria, then please let me know what caused you to answer the way you did (e.g.; you feel additional laboratory tests would be needed in order to identify causality).

If, for some reason, you answer "**Yes**" to all four questions, but you still think you should check the "**No**" box, please describe your reservations or concerns.

Finally, there is space at the end of the list for any **additional** preventable drug-related morbidities in older adults that you feel are important to add.

Thank you.

Geriatric Medicine Expert Panel Survey

Please read the following **outcomes** and **patterns of care** and answer the following questions:

1. *For most older persons, should health professionals (MDs, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care?*
2. *For most older persons, should health professionals be able to **foresee the possibility of the outcome,** if those problems were not resolved?*
3. *Should most health professionals see **how to change** the pattern of care to prevent the outcome?*
4. *Should most health professionals **actually change** the pattern of care?*

If you answer "**Yes**" to all four of these questions, then this is a type of preventable drug-related morbidity and you should check the "**Yes**" box.

If you answer "**No**" to one or more of these questions, then this is **not** a type of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why.

Start of Survey

1. This **outcome** has occurred after the pattern of care below:
   Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia
   This is the **pattern of care**:
   1. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 1 month
   2. No concurrent use of a cytoprotective agent (misoprostol)
   3. Hemoglobin/ hematocrit/CBC not done within 30 days of start of therapy or not done at least every 3 months thereafter

   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

2. This **outcome** has occurred after the pattern of care below:
   ER visit/ hospitalization due to congestive heart failure and/or fluid overload
   This is the **pattern of care**:
   1. History/diagnosis of high blood pressure (over 140/90) and/or congestive heart failure
   2. NSAID (e.g.; diclofenac, indomethacin, ketoprofen, etc.) use for at least 3 months

   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

3. This **outcome** has occurred after the pattern of care below:
   Acute renal failure and/or renal insufficiency
   This is the **pattern of care**:
   1. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 3 months
   2. BUN/Serum creatinine not done at least every 3 months.

   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

4. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to extreme hypoglycemia
   This is the **pattern of care**:
   1. History/diagnosis of diabetes
   2. Use of a beta-adrengeric blocking agent (e.g.; propranolol, nadolol, etc.)

   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

5. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
   This is the **pattern of care**:
   1. History/diagnosis of depression
   2. Use of a moderate to high lipophilic beta-adrengeric blocking agent (e.g.; propranolol, pindolol, etc.)

   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

6. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
   This is the **pattern of care**:
   1. History/diagnosis of depression
   2. Use of a long-acting benzodiazepine (e.g.; Librium, Valium, Centrax, Paxipam, Dalmane, Azaene/Tranxene, etc.)

   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

7. This **outcome** has occurred after the pattern of care below:
   Digoxin toxicity
   This is the **pattern of care**:
   1. Use of digoxin
   2. BUN/serum creatinine not done at least every 6 months
   3. Digoxin level not done at least every 6 months
   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

8. This **outcome** has occurred after the pattern of care below:
   Fall and/or hip fracture and/or other bone fracture and/or bone break
   This is the **pattern of care**:
   1. Use of a tricyclic antidepressant (e.g.; amitriptyline, doxepin, imipramine, etc.)
   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

9. This **outcome** has occurred after the pattern of care below:
   Fall and/or hip fracture and/or other bone fracture and/or bone break
   This is the **pattern of care**:
   1. Use of an anti-parkinsonian agent (e.g.; levodopa, bromocriptine, benztropine, etc.)
   Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
   If no, then please explain:

   _____

10. This **outcome** has occurred after the pattern of care below:
    Fall and/or hip fracture and/or other bone fracture and/or bone break
    This is the **pattern of care**:
    1. Use of a nitrate (e.g.; isosorbide, etc.)
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

11. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization for hypokalemia
    This is the **pattern of care**:
    1. Use of a potassium-wasting diuretic (e.g.; hydrochlorothiazide, etc.)
    2. No concurrent use of potassium chloride supplement
    3. Electrolytes not checked at least every 2 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

12. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to worsening renal impairment and/or acute renal failure and/or renal insufficiency
    This is the **pattern of care**:
    1. Diagnosis/history of moderate to severe renal impairment and/or history of kidney disease
    2. Use of tetracycline
    3. BUN/serum creatinine not done within 30 days of initiation of therapy and at least every 6 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

13. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to hyperkalemia
    This is the **pattern of care**:
    1. Use of an ACE inhibitor (e.g.; captopril, enalapril, etc.)
    2. Electrolytes/CBC not done at least every 6 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

14. This **outcome** has occurred after the pattern of care below:
    Blood dyscrasias and/or hyponatremia and/or excessive water retention and/or syndrome of inappropriate antidiuretic hormone (SIADH)
    This is the **pattern of care**:
    1. Use of carbamazepine
    2. Electrolytes/CBC not done before therapy initiated, at least weekly during the first month of therapy, at least monthly during the next five months of therapy, and at least every 6 months thereafter
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

15. This **outcome** has occurred after the pattern of care below:
    Acute renal failure and/or renal insufficiency
    This is the **pattern of care**:
    1. Use of allopurinol
    2. BUN/serum creatinine not done at least every 6 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

16. This **outcome** has occurred after the pattern of care below:
    Acute renal failure and/or renal insufficiency
    This is the **pattern of care**:
    1. Use of lithium
    2. BUN/serum creatinine not done at least every 3 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

17. This **outcome** has occurred after the pattern of care below:
    Anticonvulsant drug toxicity
    This is the **pattern of care**:
    1. Use of an anticonvulsant requiring drug level monitoring (e.g.; phenytoin, carbamazepine, valproic acid)
    2. Drug level not done at least every 6 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

18. This **outcome** has occurred after the pattern of care below:
    Theophylline toxicity
    This is the **pattern of care**:
    1. Use of theophylline
    2. Drug level not done at least every 6 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

19. This **outcome** has occurred after the pattern of care below:
    Bipolar exacerbation and/or ER visit/hospitalization due to bipolar disorder
    This is the **pattern of care**:
    1. Diagnosis/history of bipolar disorder
    2. Use of lithium
    3. Drug level not done at least every 3 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

20. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to hypoglycemia or hyperglycemia
    This is the **pattern of care**:
    1. Use of insulin
    2. Hemoglobin A1c level not done at least every 6 months
    Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
    If no, then please explain:

    _____

21. This **outcome** has occurred after the pattern of care below:
Major and/or minor hemorrhagic event
This is the **pattern of care**:
1. Use of SQ heparin
2. PTT not done at least every month
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

22. This **outcome** has occurred after the pattern of care below:
Major and/or minor hemorrhagic event
This is the **pattern of care**:
1. Use of IV heparin
2. PTT not done at least every day
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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23. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hypothyroidism
This is the **pattern of care**:
1. Use of a thyroid or antithyroid agent (e.g.; levothyroxine, propylthiouracil, etc.)
2. T4/TSH not done before therapy starts and at least every 12 months thereafter
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

24. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to systolic heart failure
This is the **pattern of care**:
1. History/diagnosis of systolic heart failure
2. Use of a beta-adrengeric blocking agent (e.g.; propranolol, nadolol, etc.)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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25. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure
This is the **pattern of care**:
1. History/diagnosis of congestive heart failure
2. Use of an antiarrhythmic agent (e.g.; disopyramide, procainamide, etc.)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

26. This **outcome** has occurred after the pattern of care below:
Gastritis and/or upper GI bleeds and/or GI perforations and/or GI ulcers and anemia
This is the **pattern of care**:
1. History/diagnosis of ulcers and/or gastrointestinal bleeding
2. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 1 month
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

_____

27. This **outcome** has occurred after the pattern of care below:
Acute renal failure and/or renal insufficiency
This is the **pattern of care**:
1.NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 3 months
2.BUN/serum creatinine not done when therapy starts and at least every 3 months thereafter
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

_____

28. This **outcome** has occurred after the pattern of care below:
Gastritis and/or upper GI bleeds and/or GI perforations and/or GI ulcers and anemia
This is the **pattern of care**:
1. History/diagnosis of ulcers and/or gastrointestinal bleeding
2. Use of an oral corticosteroid (e.g., prednisone) for at least 3 months
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

_____

29. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
This is the **pattern of care**:
1. History/diagnosis of depression
2. Use of a barbiturate (e.g.; butalbital)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

_____

30. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
This is the **pattern of care**:
1. History/diagnosis of depression
2. Use of a sympatholytic antihypertensive (e.g.; resperine, methyldopa, clonidine, etc.)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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31. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure and/or heart block
This is the **pattern of care**:
1. History/diagnosis of congestive heart failure with heart block or advanced bradycardia
2. Use of digoxin
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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32. This **outcome** has occurred after the pattern of care below:
Fall and/or hip fracture and/or other bone fracture and/or bone break
This is the **pattern of care**:
1. Use of a long-half-life hypnotic-anxiolytic (e.g.; flurazepam, diazepam, chlordiazepoxide, etc.)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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33. This **outcome** has occurred after the pattern of care below:
Fall and/or hip fracture and/or other bone fracture and/or bone break
This is the **pattern of care**:
1. Use of an antipsychotic (e.g.; thioridazine, haloperidol, chlorpromazine, etc.)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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34. This **outcome** has occurred after the pattern of care below:
Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization due to asthma
This is the **pattern of care**:
1. Diagnosis of asthma
2. Use of a bronchodilator
3. No use of a maintenance corticosteriod (e.g.; beclomethasone, etc.)
Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

35. This **outcome** has occurred after the pattern of care below:
Hospitalization/ER visit due to worsening renal impairment and/or acute renal failure and/or renal insufficiency
This is the **pattern of care**:
1. Diagnosis/history of moderate to severe renal impairment/history of kidney disease
2. Use of a select urinary antiinfective agent (nalidixic acid, nitrofurantoin or methenamine complexes)
3. BUN/serum creatinine not done within 30 days of initiation of therapy and at least every six months

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

36. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure
This is the **pattern of care**:
1. Diagnosis/history of congestive heart failure
2. Not on an ACE inhibitor (e.g.; captopril, enalapril, etc.)

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

37. This **outcome** has occurred after the pattern of care below:
Acute renal failure and/or renal insufficiency
This is the **pattern of care**:
1. Use of an ACE inhibitor (e.g.; captopril, enalapril, etc.)
2. BUN/serum creatinine not done at initiation of therapy and at least every 3 months thereafter

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

38. This **outcome** has occurred after the pattern of care below:
Aminoglycoside toxicity (acute renal failure and/or renal insufficiency and/or vestibular damage and/or auditory damage)
This is the **pattern of care**:
1. Use of an aminoglycoside
2. Serum creatinine not done before and after therapy (and if therapy longer than 7 days, not done at least every 7 days)
3. At least one drug level not done

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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39. This **outcome** has occurred after the pattern of care below:
Status epilepticus and/or ER visit/hospitalization due to seizure activity
This is the **pattern of care**:
1. Use of an anticonvulsant requiring drug level monitoring (e.g.; phenytoin, carbamazepine, valproic acid)
2. Drug level not done upon initiation of therapy and at least every 6 months thereafter

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

40. This **outcome** has occurred after the pattern of care below:
Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization due to asthma
This is the **pattern of care**:
1. Diagnosis of asthma
2. Use of theophylline
3. Drug level not done at least every 6 months

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

41. This **outcome** has occurred after the pattern of care below:
Lithium toxicity
This is the **pattern of care**:
1. Use of lithium
2. Lithium level not done at least every month

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

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42. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hyperglycemia
This is the **pattern of care**:
1. Use of an oral hypoglycemic agent (e.g.; chlorpropamide, etc.)
2. Hemoglobin A1c level not done at least every 6 months

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

43. This **outcome** has occurred after the pattern of care below:
Major and/or minor hemorrhagic event
This is the **pattern of care**:
1. Use of warfarin
2. Prothrombin time not done before therapy starts and at least every month thereafter

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

44. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hyperthyroidism
This is the **pattern of care**:
1. Use of a thyroid or antithyroid agent (e.g.; levothyroxine, propylthiouracil, etc.)
2. T4/TSH not done within 6 weeks after initiation of therapy and at least every 12 months thereafter

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

45. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure
This is the **pattern of care**:
1. History/diagnosis of congestive heart failure
2. Use of a calcium channel blocker (e.g.; diltiazem, etc.)

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

46. This **outcome** has occurred after the pattern of care below:
Secondary myocardial infarction
This is the **pattern of care**:
1. History/diagnosis of myocardial infarction
2. No use of ASA and/or a beta-blocker (e.g.; metoprolol, etc.)

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

47. This **outcome** has occurred after the pattern of care below:
Blood dyscrasias
This is the **pattern of care**:
1. Concurrent use of trimethoprim/ sulfamethoxazole (Bactrim, Septra) and methotrexate
2. WBC/platelets/CBC not done at least every 4 weeks

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐
If no, then please explain:

---

48. This **outcome** has occurred after the pattern of care below:

COPD exacerbation and/or ER visit/hospitalization due to COPD

This is the **pattern of care**:

1. Diagnosis/history of COPD
2. Use of a beta-blocker (e.g.; propranolol, etc.)

Is this a type of *preventable* drug-related morbidity? Yes ☐ No ☐

If no, then please explain:

_____

Please describe any additional preventable drug-related morbidities that you believe occur in older persons:

1. Outcome:_____
   Pattern of care:_____
   _____
2. Outcome:_____
   Pattern of care:_____
   _____
3. Outcome:_____
   Pattern of care:_____
   _____

Thank you. Please fax to Neil MacKinnon by Friday, July 31 at (352) 392-7782.

APPENDIX C
INSTRUCTIONS FOR PATIENT CHART ABSTRACTER, PATIENT CHART ABSTRACT FORM, AND SAMPLE PATIENTS

Instructions for Patient Chart Abstracter

1. I have provided you with a list of Premier Care Plan patients who were found to have diagnosis codes related to either hyperglycemia or secondary myocardial infarction. In this list, you were given the patient's medical record number and the date of the outcome event. Some of these patients met our criteria for preventable drug-related morbidity and some do not. You were not told whether these patients did, in fact, have a case of preventable drug-related morbidity.
2. Write down the outcome event (either hyperglycemia or secondary MI). The patient will likely have other diagnoses/procedures but do not list them here.
3. Write a description of the pattern of care that proceeded the outcome event. This description can follow the same format that you would use if you were presenting a case study to medical grand rounds or a pharmacy in-service. Make sure to include the following things: (1) any relative patient demographics, (2) chief compliants of the patient, (3) patient's past medical history, (4) the diagnoses made /procedures done, (5) the patient's medications upon admission, and (6) any other information you deem to be necessary or relevant, using your clinical judgement. Total length of the description should not exceed one page.
4. For patients with the outcome of hyperglycemia, be sure to include the following information: (1) use, if any, of oral hypoglycemic agents prior to admission, and (2) dates when a hemoglobin A1c level was performed. Specifically, we are interested in whether the patient had this test done at least every 6 months. Please document this clearly in the chart abstract.
5. For patients with the outcome of secondary MI, be sure to document (1) whether the patient did indeed have a previous MI, (2) use, if any, of ASA prior to admission, and (3) use, if any, of a beta-blocker prior to admission.
6. On the reverse side of the form, please document the patient's medical record number.
7. I will review two sample cases with you before you begin the patient chart abstracting process to familiarize you with the chart abstract form.
8. Feel free to contact me if you have any questions:

Neil MacKinnon, M.S., R.Ph.
Work Phone: (352) 846-0163
Home Phone: (352) 336-8348
Fax: (352) 392-7782
E-mail:neil@cop3.health.ufl.edu

Drug Therapy Risk Assessment and Management Program

(DT-RAMP) Patient Chart Abstract Form

Outcome Event:_____

Description of the pattern of care that preceded the outcome event:_____

Please review the above patient chart abstract and answer the following questions to judge whether this was a case of preventable drug-related morbidity:

1. Should health professionals (MDs, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care (related to the above outcome)?
2. Should health professionals be able to **foresee the possibility** of the above outcome in this patient?

3. Should most health professionals **see how to change** the pattern of care to prevent the above outcome in this patient?
4. Should most health professionals **actually change** the pattern of care in this patient?

If you answer "**Yes**" to all four of these questions, then this is a case of preventable drug-related morbidity and you should check the "**Yes**" box.

If you answer "**No**" to one or more of these questions, then this is not a case of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why.

Is this a case of preventable drug-related morbidity? Yes □ No □

If no, then please explain:

_____

Drug Therapy Risk Assessment and Management Program (DT-RAMP) Patient Chart Abstract Form – Example of a preventable drug-related morbidity

Outcome Event: LM admitted to Florida Hospital on 10/10/97 with an upper GI bleed

Description of the pattern of care that preceded the outcome event: LM is a 68 y/o WF with a history of arthritis and hypertension. She is admitted to Florida Hospital with an upper GI bleed. Her physical examination is within normal limits. Her medications upon admission are diclofenac 50 mg tid for arthritis and furosemide 20 mg qam for hypertension. She is not receiving any cytoprotective agents. Her hemoglobin and hematocrit are done upon admission and are 14.2 gm/dl and 44%, respectively. Before that, her last documented hematocrit is from 11/11/96. LM noticed some blood in her urine over the past few weeks and noted recently that her stools have become black and tarry in appearance but she has no other symptoms consistent with peptic ulcer disease.

Please review the above patient chart abstract and answer the following questions to judge whether this was a case of preventable drug-related morbidity:

1. Should health professionals (MDs, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care (related to the above outcome)? *(yes- NSAID use without a cytoprotective agent or regular hematocrits)*
2. Should health professionals be able to **foresee the possibility** of the above outcome in this patient? *(yes- patient is an older adult and is therefore at an increased risk of a GI bleed)*
3. Should most health professionals **see how to change** the pattern of care to prevent the above outcome in this patient? *(yes – could add a cytoprotective agent, do regular hematocrits or even change diclofenac to a different drug)*
4. Should most health professionals **actually change** the pattern of care in this patient? *(yes – could do any of the above things)*

If you answer "**Yes**" to all four of these questions, then this is a case of preventable drug-related morbidity and you should check the "**Yes**" box.

If you answer "**No**" to one or more of these questions, then this is not a case of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why.

Is this a case of preventable drug-related morbidity? Yes ✓ No □

If no, then please explain:

_____

Drug Therapy Risk Assessment and Management Program (DT-RAMP) Patient Chart Abstract Form – Example of a patient without preventable drug-related morbidity

Outcome Event: LM admitted to Florida Hospital on 10/10/97 with an upper GI bleed
Description of the pattern of care that preceded the outcome event: LM is a 68 y/o WF with a history of arthritis and hypertension. She is admitted to Florida Hospital with an upper GI bleed. Her physical examination is within normal limits. Her medications upon admission are diclofenac 50 mg tid for arthritis, misoprostol 200 mcg qid for GI protection and furosemide 40 mg qam for hypertension. Her hemoglobin and hematocrit are done upon admission and are 14.2 gm/dl and 44%, respectively. Her physician, Dr. Perry Colace has ordered hematocrits every 3 months, the last one being done on 09/09/99. LM noticed some blood in her urine over the past few weeks and noted recently that her stools have become black and tarry in appearance but she has no other symptoms consistent with peptic ulcer disease.

Please review the above patient chart abstract and answer the following questions to judge whether this was a case of preventable drug-related morbidity:

1. Should health professionals (MDs, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care (related to the above outcome)? *(no- pt on a NSAID but also receiving a cytoprotective agent and regular hematocrits – proper pattern of care)*
2. Should health professionals be able to **foresee the possibility** of the above outcome in this patient? *(yes- patient is an older adult and is therefore at an increased risk of a GI bleed)*
3. Should most health professionals **see how to change** the pattern of care to prevent the above outcome in this patient? *(no– already on a cytoprotective agent and getting regular hematocrits - could possibly change diclofenac to a different drug)*
4. Should most health professionals **actually change** the pattern of care in this patient? *(yes – could change diclofenac to a different drug – may work)*

If you answer "**Yes**" to all four of these questions, then this is a case of preventable drug-related morbidity and you should check the "**Yes**" box.

If you answer "**No**" to one or more of these questions, then this is not a case of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why.

Is this a case of preventable drug-related morbidity? Yes ☐ No ✓

If no, then please explain:

GI bleed may be due to NSAID use, but Dr. Colace took precautions with adding misoprostol for GI protection and regular hematocrits for monitoring; therefore it was not a case of *preventable* drug-related morbidity.

APPENDIX D
MEMBERS OF THE CHART ABSTRACT REVIEWER PANEL

Category	Pharmacist # 1	Pharmacist #2	Pharmacist #3
Name	Helen Hsu	Robert Vandervort	John (Bill) Kennedy
Degree(s)	Pharm.D.	Pharm.D.	Pharm.D.
Years of Clinical Experience	5	3	18
Areas with clinical expertise	Internal Medicine	Family Practice	Family Practice
Experience reading chart abstracts	Y	Y	Y
Experience completing ADR forms (MedWatch, etc.)	Y	Y	N
Category	Pharmacist #4	Pharmacist #5	
Name	Sandra Newman	Simone Minto-Pennant	
Degree(s)	Pharm.D.	Pharm.D., C.Ph.	
Years of Clinical Experience	7	1	
Areas with clinical expertise	Geriatrics	Geriatrics, Inpatient & Family Practice	
Experience reading chart abstracts	Y	Y	
Experience completing ADR forms (MedWatch, etc.)	Y	Y	

APPENDIX E
INSTRUCTIONS FOR CHART ABSTRACT REVIEWER PANEL

November 6, 1998

Dear Chart Abstract Reviewer Panel Member,

As you know, a major problem in the health of older persons is *preventable* drug-related morbidity. Your expertise will be used to determine whether the patients described in the following chart abstracts experienced a preventable drug-related morbidity.

Your input is important, as there are only four members of the Chart Abstract Reviewer Panel. Please return the patient chart abstract forms with your responses to Scott Neel by **Tuesday, November 10, 1998** to ensure that your input is considered.

Feel free to call Scott Neel with any questions at extension 6338 or Neil MacKinnon at (352) 846-0163. Again, thank you.

Sincerely,

Scott A. Neel, Pharm.D.
Primary Care Resident

Neil J. MacKinnon, M.S., R.Ph.
Ph.D. Candidate and Research Fellow

Instructions

You have been given chart abstracts from older persons who were admitted to the Florida Hospital in 1997 with one of two diagnoses: hyperglycemia or secondary myocardial infarction. Some of these patients met our criteria for a preventable drug-related morbidity and some did not.

● In order to evaluate whether these patients experienced a *preventable drug-related morbidity* or not, you should read the **outcome event** and **description of the pattern of care that preceded the outcome event** and answer the following questions:

*1. Should health professionals (MDs, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care (related to the above outcome)?*

*2. Should health professionals be able to **foresee the possibility** of the above outcome in this patient?*

*3. Should most health professionals see **how to change** the pattern of care to prevent the above outcome in this patient?*

*4. Should most health professionals **actually change** the pattern of care in this patient?*

● If you answer "**Yes**" to all four of these questions, then this is a type of preventable drug-related morbidity and you should check the "**Yes**" box.

● If you answer "**No**" to one or more of these questions, then this is **not** a type of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why. This section is very important to complete. Please be as specific as you possibly can.

If, for some reason, you answer "**Yes**" to all four questions, but you still think you should check the "**No**" box, please describe your reservations or concerns.

Thank you.

APPENDIX F
PERSONAL WELLNESS PROFILE SENIOR ASSESSMENT

Gender

(1) Male

(2) Female

Age years

Height Feet, inches

Weight Pounds

Questions:

1. **Health.** In general, would you say your health is:

(1) excellent

(2) very good

(3) good

(4) fair

(5) poor

2. **General Health**. Compared to one year ago, how would you rate your health in general now?

(1) much better now than one year ago

(2) somewhat better now than one year ago

(3) about the same

(4) somewhat worse now than one year ago

(5) much worse now than one year ago

3. **Bodily pain**. How much bodily pain have you had during the past four weeks?

   (1) none

   (2) very mild

   (3) mild

   (4) moderate

   (5) severe

   (6) very severe

4. **Health view**. Mark any of the following that apply to you.

   (1) I'm as healthy as anybody I know.

   (2) I seem to get sick a little easier than other people.

   (3) I expect my health to get worse.

   (4) I have a serious health problem.

5. **Health limitations**. During the past four weeks, how much difficulty did you have doing your work or other regular daily activities as a result of your physical health?

   (1) none at all

   (2) a little bit

   (3) some

   (4) quite a bit

   (5) could not do daily work

6. **Emotional problems**. During the past four weeks, to what extent have you accomplished less than you would like in your work or other daily activities as a result of emotional problems, such as feeling depressed or anxious?

   (1) none at all

   (2) slightly

   (3) moderately

   (4) quite a bit

   (5) extremely

7. **Social activity**. During the past four weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

   (1) not at all

   (2) slightly

   (3) moderately

   (4) quite a bit

   (5) extremely

8. **Daily activities.** The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

   1: yes, limited a lot

   2: yes, limited a little

   3: no ,not limited at all

   1 - (1)(2)(3) lifting or carrying groceries

   2 - (1)(2)(3) climbing several flights of stairs

   3 - (1)(2)(3) walking several blocks

9. **Feelings**. The next questions are about how you feel things have been with you during the past four weeks. For each question, please give the one answer that comes the closest to the way you have been feeling. How much of the time during the past four weeks…

   1: all the time

   2: most of the time

   3: a good bit of the time

   4: some of the time

   5: a little of the time

   6: none of the time

   1 - (1)(2)(3)(4)(5)(6) Have you felt calm and peaceful?

2 - (1)(2)(3)(4)(5)(6) Did you have a lot of energy?

3 - (1)(2)(3)(4)(5)(6) Have you felt downhearted and blue?

4 - (1)(2)(3)(4)(5)(6) Have you been a happy person?

10. **Eating habits**. The following items relate to your eating habits. Mark any item that is true for you or describes your current situation.

1 - I have an illness or condition that has made me change the kind or amount of food I eat.

2 - I eat fewer than two meals per day.

3 - I eat few fruits or vegetables, or milk products.

4 - I have three or more drinks of beer, liquor, or wine almost every day.

5 - I have tooth or mouth problems that make it hard for me to eat.

6 - I don't always have enough money to buy the food I need.

7 - I eat alone most of the time.

8 - Without wanting to, I have lost or gained 10 pounds in the last 6 months.

9 - I am not always physically able to shop, cook, and/or feed myself.

11. **Health practices**. The following questions refer to common health practices. Please answer **yes** or **no**. Do you…

1: yes 2: no

1 - (1)(2) currently smoke?

2 - (1)(2) often use medicines that affect your mood, help you relax or sleep?

3 - (1)(2) often have more than 1 to 2 alcoholic drinks in a day?

4 - (1)(2) usually get 7 to 8 hours sleep daily (including naps)?

5 - (1)(2) ever drive after drinking?

6 - (1)(2) consider yourself more than 20 pounds overweight?

7 - (1)(2) always wear your seat belt when driving or riding in a car?

8 - (1)(2) usually eat breakfast?

9 - (1)(2) eat primarily whole-grain breads and cereals?

10 - (1)(2) make a serious attempt to eat primarily low fat foods?

11 - (1)(2) regularly snack on junk foods (chips, doughnuts, cookies, candy)?

12 - (1)(2) have a working smoke alarm at home?

13 - (1)(2) always do heavy lifts with legs and not back?

14 - (1)(2) cope well with stress in your life?

12. **Exercise**. How many days per week do you engage in aerobic exercise of at least 20 to 30 minutes duration (Brisk walking, golf [walking, no cart] dancing, active gardening, cycling, swimming, etc.)?

(1) none

(2) one to two

(3) three to four

(4) five or more

13. **Fruits and vegetables**. How many servings of fruits and vegetables do you usually eat per day?

(1) one or less

(2) two

(3) three

(4) four

(5) five or more

14. **Personal health history**. Has a doctor informed you that you currently have any of the following health problems? **If yes**, mark either **yes, but not taking** or **yes, and taking medication**, otherwise leave blank.

1: yes, not taking medication 2: yes, taking medication

1 - (1)(2) arthritis

2 - (1)(2) bladder or bowel control problems

3 - (1)(2) blind/trouble seeing, even with glasses

4 - (1)(2) cancer, other than skin cancer (within last 5 years)

5 - (1)(2) congestive hear failure

6 - (1)(2) heart attack, angina, by-pass surgery, or angioplasty

7 - (1)(2) chronic back problems or sciatica

8 - (1)(2) deafness or trouble hearing

9 - (1)(2) diabetes (high blood sugar)

10 - (1)(2) high blood pressure (140/90 or higher)

11 - (1)(2) lung disease, emphysema, bronchitis, or asthma

12 - (1)(2) memory problems (more than typical)

13 - (1)(2) kidney disease

14 - (1)(2) stroke

15 - (1)(2) ulcer or gastrointestinal bleeding

15. **Social health**. Answer the following questions with a yes or no.

1: yes 2: no

1 - (1)(2) Do you participate in church or community activities regularly with your friends?

2 - (1)(2) Do you have a plan for getting emergency help if you need it?

3 - (1)(2) Do you feel overwhelmed by a recent crisis or loss?

4 - (1)(2) Have you recently considered ending your life?

16. **Living arrangements**. I live with…

(1) my spouse

(2) by myself

(3) a paid caregiver

(4) family/relatives

(5) a friend

(6) other

17. **Hospital**. How many times were you hospitalized in the last 12 months?

(1) none

(2) one to two

(3) three or more

18. **Emergency Room**. How many times did you seek care in the emergency room in the last 12 months?

(1) none

(2) one to two

(3) three or more

19. **Doctor visits**. How many times did you visit a doctor in the last 12 months?

(1) none

(2) one to two

(3) three to four

(4) five or more

20. **Nursing Home**. In the past year, have you been admitted to a nursing or convalescent home?

(1) yes

(2) no

21. **Prescription drugs**. How many different prescribed drugs do you take daily?

(1) none

(2) one to two

(3) three to five

(4) six or more

22. **Over-the-counter drugs**. How many different over-the-counter drugs do you take daily? (mark one)

(1) none

(2) one to two

(3) three to five

(4) six or more

23. **Medicines**. Do you have trouble paying for your medicines?

(1) yes

(2) only some times

(3) no or not applicable

24. **Falling**. Have you fallen in the last year (how often)?

(1) no

(2) yes, 1 to 2 times

(3) yes, 3 or more times

25. **Medical equipment**. Are you currently using medical equipment, for example: oxygen, hospital bed, wheelchair, walker.

(1) yes

(2) no

26. **Home health services**. Are you currently receiving home health services, such as: visiting nurse, physical therapy, homemaker/aids, adult day care, etc.

(1) yes

(2) no

27. **Physical health**. Think about your physical health, including illness and injury. How many days during the last 30 days was your physical health not good?

(1) none

(2) one to two

(3) three to five

(4) six or more

28. **Mental health**. Think about your mental health, including stress, depression, and problems with emotions. How many days during the last 30 days was your mental health not good?

(1) none

(2) one to two

(3) three to five

(4) six or more

29. **Blood pressure**. Do you have a blood pressure of 140/90 or higher?

(1) yes

(2) no

(3) don't know

30. **Cholesterol.** Do you have a cholesterol level of 200 or higher?

(1) yes

(2) no

(3) don't know

31. **Activities of daily living**. How difficult are the following activities and tasks for you?

1: not difficult 2: difficult 3: very difficult or can't do it

1 - (1)(2)(3) bathing

2 - (1)(2)(3) dressing

3 - (1)(2)(3) getting out of bed

4 - (1)(2)(3) getting out of a chair

5 - (1)(2)(3) eating

6 - (1)(2)(3) using the toilet

7 - (1)(2)(3) walking around the house

8 - (1)(2)(3) shopping and errands

9 - (1)(2)(3) housekeeping

10 - (1)(2)(3) preparing meals

11 - (1)(2)(3) doing laundry

12 - (1)(2)(3) using the telephone

13 - (1)(2)(3) taking medications

14 - (1)(2)(3) using transportation

15 - (1)(2)(3) managing your money

32. **Physical exam**. When was your last physical examination? Within the last…

(1) year

(2) 2 years

(3) 3 years

(4) 4 years

(5) 5 years or more

33. **Preventive exams**. Mark the preventive exams you have had during the time frame listed (leave blank if you are not sure).

1 - cholesterol check, within the last 2-5 years

2 - blood pressure check, every 1-2 years

3 - check for blood in stool yearly, or bowel exam with flexible sigmoidoscopy every 3-10 years

4 - dental exam, yearly

5 - vision, every 2 years

6 - hearing, periodically as needed

7 - health-lifestyle assessment, every 1-2 years

8 - tetanus shot, every 10 years

9 - pneumonia immunization, once

10 - flu shot, yearly

11 - PAP smear, every 1-3 years

12 - mammogram with breast exam, every 1-2 years up to age 69

13 - breast self-exam, monthly

14 - PSA and rectal exam every 1-2 years

34. **Race**. Mark one.

(1) Native American

(2) Asian

(3) African-American, black

(4) Caucasian, white

(5) Hispanic

(6) Other

35. **Living will**. Have you completed a living will or advance directive? (A statement prepared when a person is well and competent to give guidance to the health care team concerning the person's wishes regarding heroics for life support in a terminally ill condition when such treatment will not permit recovery, or give authority to another person to make these decisions if they are in a coma.)

(1) yes

(2) no

36. **Readiness to change**. Mark the response below that best describes where you are currently in relation to adopting a healthier lifestyle.

(1) I don't think I will make any changes this year.

(2) I plan on adopting a healthier lifestyle in the next six months.

(3) I plan on adopting a healthier lifestyle this month.

(4) I've adopted a healthier lifestyle in the last six months.

(5) I've lived a healthy lifestyle for over six months.

37. **Health interest survey**. Mark any of the following health improvement opportunities that you would like to be notified about if available.

(1) Help quitting smoking

(2) Weight management

(3) Aerobic exercise to music

(4) A walking group

(5) A jogging group

(6) a fitness evaluation

(7) Nutrition improvement

(8) Cholesterol reduction

(9) Blood pressure control

(10) Coronary risk reduction

(11) Cancer risk reduction

(12) Alcohol/drug awareness

(13) Healthy back program

(14) Medical self-care

(15) Stress management

(16) CPR training

(17) First aid

(18) Comprehensive health evaluation

(19) Women's health programs

(20) Relationship enrichment

(21) Retirement planning

(22) Living wills/advance directives

1 - Do not notify me about health improvement opportunities

38. When is the best time to contact you?

(1) morning

(2) afternoon

(3) evening

Additional Drug-Related Questions

1. Are you taking any of the following medications? (Mark all that apply)

(1) Warfarin (Coumadin®)

(2) Theophylline (Theodur®, Slophyllin®, Theo-24®, Uniphyl®, Theolair®)

(3) Digoxin (Lanoxin®, Lanoxicap®)

(4) Cimetidine (Tagamet®)

(5) Not on any of these medications

2. Are you taking of the following medications? (Mark all that apply.)

(1) Phenytoin (Dilantin®)

(2) Carbamazepine (Tegretol®)

(3) Phenobarbital

(4) Valproic Acid (Depakote®, Depakene®)

(5) Not on any of these medications.

3. Have you had a side effect due to a medication that caused you to stop that medication in the last 6 months?

(1) Yes

(2) No

4. How do you feel about the number of medications that you are taking?

(1) Not currently taking any medications.

(2) The number of medications I am taking is about right.

(3) I think the number of medications I am taking is too many.

APPENDIX G
ROUND 3 OF THE GERIATRIC MEDICINE EXPERT PANEL SURVEY

Geriatric Medicine Expert Panel Survey – Round 3: Final Results

The following outcomes & patterns of care were agreed to be preventable drug-related morbidities by all 7 geriatric medicine expert panel members:

1. This **outcome** has occurred after the pattern of care below:
   Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia
   This is the **pattern of care**:
   1. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 1 month
   2. No concurrent use of a cytoprotective agent (misoprostol)
   3. Hemoglobin/ hematocrit/CBC not done within 30 days of start of therapy or not done at least every 3 months thereafter

   Comments from round 1:
   But cytoprotective agents may not prevent the adverse outcome.
   (2) and (3) not necessary in every instance.

2. This **outcome** has occurred after the pattern of care below:
   Acute renal failure and/or renal insufficiency
   This is the **pattern of care**:
   1. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 3 months
   2. BUN/Serum creatinine not done at least every 3 months.

   Comments from round 1:
   Serum creatinine more than every 3 months.
   Not so neatly predictable – prefer baseline labs and then monitor clinically.
   What's baseline BUN/creatinine?

   Comments from round 2:
   Should not apply to sporadic or very low dose NSAID use.

3. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
   This is the **pattern of care**:
   1. History/diagnosis of depression
   2. Use of a long-acting benzodiazepine (e.g.; Librium, Valium, Centrax, Paxipam, Dalmane, Azaene/Tranxene, etc.)

4. This **outcome** has occurred after the pattern of care below:
   Fall and/or hip fracture and/or other bone fracture and/or bone break
   This is the **pattern of care**:
   1. Use of a tricyclic antidepressant (e.g.; amitriptyline, doxepin, imipramine, etc.)
   Comments from round 1:
   May not apply to low-dose analgesic doses.

5. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to worsening renal impairment and/or acute renal failure and/or renal insufficiency
   This is the **pattern of care**:
   1. Diagnosis/history of moderate to severe renal impairment and/or history of kidney disease
   2. Use of tetracycline
   3. BUN/serum creatinine not done within 30 days of initiation of therapy and at least every 6 months
   Comments from round 1:
   Chronic tetracycline? E.g.; For acne?
   Use serum creatinine.

6. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to hyperkalemia
   This is the **pattern of care**:
   1. Use of an ACE inhibitor (e.g.; captopril, enalapril, etc.)
   2. Electrolytes/CBC not done at least every 6 months
   Comments from round 1:
   Should be done baseline, 10-14 days, then prn.

7. This **outcome** has occurred after the pattern of care below:
   Blood dyscrasias and/or hyponatremia and/or excessive water retention and/or syndrome of inappropriate antidiuretic hormone (SIADH)
   This is the **pattern of care**:
   1. Use of carbamazepine
   2. Electrolytes/CBC not done before therapy initiated, at least weekly during the first month of therapy, at least monthly during the next five months of therapy, and at least every 6 months thereafter
   Comments from round 1:
   I monitor only CBC and drug levels routinely; others prn.

8. This **outcome** has occurred after the pattern of care below:
   Acute renal failure and/or renal insufficiency
   This is the **pattern of care**:
   1. Use of lithium
   2. BUN/serum creatinine not done at least every 3 months
   Comments from round 1:
   Monitor lithium levels.
   The pattern of prevention should be used in those patients with baseline creatinine elevation.
   Use serum creatinine.
   Comments from round 2:
   I'll go with the group, but this is not generally the practice.
   Need to follow electrolytes also.

9. This **outcome** has occurred after the pattern of care below:
   Theophylline toxicity
   This is the **pattern of care**:
   1. Use of theophylline
   2. Drug level not done at least every 6 months
   Comments from round 1:
   Addition of other medications that interact with theophylline?

10. This **outcome** has occurred after the pattern of care below:
    Bipolar exacerbation and/or ER visit/hospitalization due to bipolar disorder
    This is the **pattern of care**:
    1. Diagnosis/history of bipolar disorder
    2. Use of lithium
    3. Drug level not done at least every 3 months
    Comments from round 1:
    Lithium level is not an all-inclusive monitoring parameter (i.e.; level may be normal).

11. This **outcome** has occurred after the pattern of care below:
    Major and/or minor hemorrhagic event
    This is the **pattern of care**:
    1. Use of IV heparin
    2. PTT not done at least every day
    Comments from round 1:
    Usually requires more frequent monitoring, at least initially.

12. This **outcome** has occurred after the pattern of care below:
    Gastritis and/or upper GI bleeds and/or GI perforations and/or GI ulcers and anemia
    This is the **pattern of care**:
    1. History/diagnosis of ulcers and/or gastrointestinal bleeding
    2. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least 1 month
    Comments from round 1:
    Cytoprotective agent!!

13. This **outcome** has occurred after the pattern of care below:
    Gastritis and/or upper GI bleeds and/or GI perforations and/or GI ulcers and anemia
    This is the **pattern of care**:
    1. History/diagnosis of ulcers and/or gastrointestinal bleeding
    2. Use of an oral corticosteroid (e.g., prednisone) for at least 3 months
    Comments from round 1:
    No proof.
    The prednisone may be essential and some antiulcer medications may interfere with its absorption – thus might want to use antiulcer medications with prednisone.
    Comments from round 2:
    Long-term corticosteriods warrant close monitoring of patient period!

14. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
    This is the **pattern of care**:
    1. History/diagnosis of depression
    2. Use of a barbiturate (e.g.; butalbital)

15. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
    This is the **pattern of care**:
    1. History/diagnosis of depression
    2. Use of a sympatholytic antihypertensive (e.g.; resperine, methyldopa, clonidine, etc.)

16. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to congestive heart failure and/or heart block
    This is the **pattern of care**:
    1. History/diagnosis of congestive heart failure with heart block or advanced bradycardia
    2. Use of digoxin
    Comments from round 1:
    What kind of monitoring? Concomitant medications? Dosage?

17. This **outcome** has occurred after the pattern of care below:
    Fall and/or hip fracture and/or other bone fracture and/or bone break
    This is the **pattern of care**:
    1. Use of a long-half-life hypnotic-anxiolytic (e.g.; flurazepam, diazepam, chlordiazepoxide, etc.)

18. This **outcome** has occurred after the pattern of care below:
Acute renal failure and/or renal insufficiency
This is the **pattern of care**:
1. Use of an ACE inhibitor (e.g.; captopril, enalapril, etc.)
2. BUN/serum creatinine not done at initiation of therapy and at least every 3 months thereafter
Comments from round 1:
Initial monitoring should be 10-14 days after starting.
Unless patient has renal insufficiency with concomitant diabetes.
Check BUN/serum creatinine every 3 – 6 months.

19. This **outcome** has occurred after the pattern of care below:
Status epilepticus and/or ER visit/hospitalization due to seizure activity
This is the **pattern of care**:
1. Use of an anticonvulsant requiring drug level monitoring (e.g.; phenytoin, carbamazepine, valproic acid)
2. Drug level not done upon initiation of therapy and at least every 6 months thereafter
Comments from round 1:
Once seizure control achieved, not necessary to obtain blood levels.

20. This **outcome** has occurred after the pattern of care below:
Lithium toxicity
This is the **pattern of care**:
1. Use of lithium
2. Lithium level not done at least every month
Comments from round 1:
Monthly too frequent for most cases.
Electrolyte (chemistry lab test) needed.
Comments from round 2:
Still think monthly too frequent in stable patient.

21. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hyperglycemia
This is the **pattern of care**:
1. Use of an oral hypoglycemic agent (e.g.; chlorpropamide, etc.)
2. Hemoglobin A1c level not done at least every 6 months
Comments from round 1:
Should try to avoid "older" hypoglycemics in elderly.

22. This **outcome** has occurred after the pattern of care below:
Major and/or minor hemorrhagic event
This is the **pattern of care**:
1. Use of warfarin
2. Prothrombin time not done before therapy starts and at least every month thereafter

23. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hyperthyroidism
This is the **pattern of care**:
1. Use of a thyroid or antithyroid agent (e.g.; levothyroxine, propylthiouracil, etc.)
2. T4/TSH not done within 6 weeks after initiation of therapy and at least every 12 months thereafter
Comments from round 1:
TSH level sufficient.

24. This **outcome** has occurred after the pattern of care below:
Secondary myocardial infarction
This is the **pattern of care**:
1. History/diagnosis of myocardial infarction
2. No use of ASA and/or a beta-blocker (e.g.; metoprolol, etc.)

25. This **outcome** has occurred after the pattern of care below:
Blood dyscrasias
This is the **pattern of care**:
1. Concurrent use of trimethoprim/ sulfamethoxazole (Bactrim, Septra) and methotrexate
2. WBC/platelets/CBC not done at least every 4 weeks
Comments from round 1:
Also electrolytes in HIV patients (potassium increases).
Need baseline CBC also.
Also need to check hepatic function periodically for methotrexate.

26. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to a major/minor hemorrhagic event
This is the **pattern of care**:
1. Warfarin use
2. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use
3. PT not done within 10 days
Comments from round 2:
Would use cytoprotection or proton-pump inhibitor
Should not use NSAIDS and warfarin unless unusual reasons to do so.

27. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hypothyroidism
This is the **pattern of care**:
1. Lithium use for at least 6 months
2. TSH not done at least every 6 months
Comments from round 2:
Or hyperthyroidism

28. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to a major/minor hemorrhagic event
This is the **pattern of care**:
1. Warfarin use
2. Antibiotic use (Bactrim, etc.)
3. PT not done within 5 days

29. This **outcome** has occurred after the pattern of care below:
Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia
This is the **pattern of care**:
1. Use of two or more NSAIDs concurrently for at least 2 weeks
Comments from round 2:
Who does this?

30. This **outcome** has occurred after the pattern of care below:
Blood dyscrasias/ thrombocytopenia
This is the **pattern of care**:
1. Use of Ticlopidine (Ticlid)
2. CBC/platelets not done at baseline, within 2 weeks of start of therapy and within 2 months

31. This **outcome** has occurred after the pattern of care below:
Rebound congestion
This is the **pattern of care**:
1. Use of a long-acting nasal spray (e.g.; oxymetazoline) for more than 3 days

32. This **outcome** has occurred after the pattern of care below:
Acute urinary retention
This is the **pattern of care**:
1. Diagnosis/ history of bladder atony due to diabetes.
2. Use of Imipramine

33. This **outcome** has occurred after the pattern of care below:
Acute respiratory failure
This is the **pattern of care**:
1. History/ diagnosis of severe COPD
2. Use of a medium to long-acting benzodiazepine
Comments from round 2:
Probably true in C02 retainers. Should not use long-acting benzodiazepines in elderly anyway.

34. This **outcome** has occurred after the pattern of care below:
Acute urinary retention
This is the **pattern of care**:
1. History / diagnosis of benign prostatic hypertropy (BPH)
2. Use of an anticholinergic agent
Comments from round 2:
Or antihistamine

35. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to liver toxicity
This is the **pattern of care**:
1. Use of troglitazone (Rezulin)
2. Liver function tests not done at baseline and at least monthly for the first 8 months of therapy and at least every 2 months for the remainder of the first year.

The following outcomes & patterns of care were agreed to be preventable drug-related morbidities by 6 geriatric medicine expert panel members:

36. This **outcome** has occurred after the pattern of care below:
ER visit/ hospitalization due to congestive heart failure and/or fluid overload
This is the **pattern of care**:
1. History/diagnosis of high blood pressure (over 140/90) and/or congestive heart failure
2. NSAID (e.g.; diclofenac, indomethacin, ketoprofen, etc.) use for at least 3 months

Comments from round 1:
Would shorten interval to 10-14 days.
ACE inhibitors, carvedilol key prophylactics. NSAIDS & uncontrolled BP are two risk factors that can also be modified.
How frequent is monitoring of blood pressure?

Comments from round 2:
As long as it is accepted that the role of NSAIDS may be minor in this setting of hypertensive cardiomyopathy or the key prophylactics may prevent the drug morbidity in the first place.
Agree with comments regarding BP control and NSAIDS.

37. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to extreme hypogylcemia
This is the **pattern of care**:
1. History/diagnosis of diabetes
2. Use of a beta-adrengeric blocking agent (e.g.; propranolol, nadolol, etc.)

Comments from round 1:
Recent data tends to indicate that beta-blockers may not reduce hypoglycemic awareness to the degree previously claimed. Thus this is a controversial area at present.
Selective versus non-selective beta-blocker? At what dosage? Dietary habits.

Comments from round 2:
See New Engl J Med article (Aug 20, 1998) on use of beta-blockers post MI – not everyone has same degree of diabetes, severity of illness, or type.

38. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to depression and/or increase in dosage of antidepressant
This is the **pattern of care**:
1. History/diagnosis of depression
2. Use of a moderate to high lipophilic beta-adrengeric blocking agent (e.g.; propranolol, pindolol, etc.)
Comments from round 1:
Discontinuing beta-blocker in lieu of stronger antidepressant treatment.
The role in beta-blocker causation of depression is probably not as significant as previously claimed – thus it is a controversial area.
Comments from round 2:
If you can avoid using a med, then it should be done.
Beta blockers not uniformally or clearly significantly associated with depression.

39. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization for hypokalemia
This is the **pattern of care**:
1. Use of a potassium-wasting diuretic (e.g.; hydrochlorothiazide, etc.)
2. No concurrent use of potassium chloride supplement
3. Electrolytes not checked at least every 2 months
Comments from round 1:
Except very low dose (6.25 or 12.5mg) HCTZ.
I would do q 4 months for thiazides and q2-3 months for loop diuretics.
Once stable, checking electrolytes every 4-6 months is adequate.
Comments from round 2:
Agree with except low-dose HCTZ.

40. This **outcome** has occurred after the pattern of care below:
Anticonvulsant drug toxicity
This is the **pattern of care**:
1. Use of an anticonvulsant requiring drug level monitoring (e.g.; phenytoin, carbamazepine, valproic acid)
2. Drug level not done at least every 6 months
Comments from round 1:
Routine levels are not necessary once seizure control achieved and no evidence of clinical toxicity.
Addition of medications that interact with anticonvulsant?
Comments from round 2:
Still stick with my original comments despite being in the minority.

41. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hypothyroidism
This is the **pattern of care**:
1. Use of a thyroid or antithyroid agent (e.g.; levothyroxine, propylthiouracil, etc.)
2. T4/TSH not done before therapy starts and at least every 12 months thereafter
Comments from round 1:
Check TSH in 6-8 weeks and every 4 months after prescription.
Monitoring should be more frequent (TSH only).
Monitoring more frequently required.
TSH is sufficient.
Comments from round 2:
Interval too long. Many patients seen with iatrogenic hypothyroidism following their annual TSH screen.

42. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to systolic heart failure
This is the **pattern of care**:
1. History/diagnosis of systolic heart failure
2. Use of a beta-adrengeric blocking agent (e.g.; propranolol, nadolol, etc.)
Comments from round 1:
Low dose beta-blockers now recommended in Class III or IV.
Comments from round 2:
Preventable if identified as the only variable.
Dosage?
Recent literature suggests beta blockers may have value in heart failure (Aug 20, NEJM, 1998)

43. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure
This is the **pattern of care**:
1. History/diagnosis of congestive heart failure
2. Use of an antiarrhythmic agent (e.g.; disopyramide, procainamide, etc.)
Comments from round 1:
Too many other factors usually involved.
There is no answer to this – is preferable to use antiarrhythmics without the significant negative inotropic effects of the agents – but the rhythm may dictate their use.
Comments from round 2:
See above.

44. This **outcome** has occurred after the pattern of care below:
Fall and/or hip fracture and/or other bone fracture and/or bone break
This is the **pattern of care**:
1. Use of an antipsychotic (e.g.; thioridazine, haloperidol, chlorpromazine, etc.)
Comments from round 1:
Benefit may outweigh risk – perhaps no choice.
The medication may be necessary for therapy and thus the adverse event potential is mitigated by the requirement for use of the agent.
Comments from round 2:
See above comments.

45. This **outcome** has occurred after the pattern of care below:
Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization due to asthma
This is the **pattern of care**:
1. Diagnosis of asthma
2. Use of a bronchodilator
3. No use of a maintenance corticosteriod (e.g.; beclomethasone, etc.)
Comments from round 1:
Inhaled not oral
This one is patient-dependent. Could apply in some.
Mild intermittent asthma does not require anti-inflammatory medication.
Comments from round 2:
Agree with comment "could apply in some": mild intermittant – no, mild, mod, severe persistant - yes

46. This **outcome** has occurred after the pattern of care below:
Hospitalization/ER visit due to worsening renal impairment and/or acute renal failure and/or renal insufficiency
This is the **pattern of care**:
1. Diagnosis/history of moderate to severe renal impairment/history of kidney disease
2. Use of a select urinary antiinfective agent (nalidixic acid, nitrofurantoin or methenamine complexes)
3. BUN/serum creatinine not done within 30 days of initiation of therapy and at least every six months
Comments from round 1:
These drugs shouldn't be used long term – sometimes low dose nitrofurantoin is for suppression but shouldn't need monitoring.
Checking of renal status for use of these drugs is not a usual procedure.
Can't remember the last time the above three antibiotics were prescribed.
Comments from round 2:
CrCl <50 nitrofurantoin and urinary antiseptics don't work.

47. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure
This is the **pattern of care**:
1. Diagnosis/history of congestive heart failure
2. Not on an ACE inhibitor (e.g.; captopril, enalapril, etc.)
Comments from round 1:
Patient-dependent; depends on type of heart disease, renal function, etc. Could be diuretics (but maybe not an adequate dosage).
Comments from round 2:
Could be on inadequate diuretics

48. This **outcome** has occurred after the pattern of care below:
Aminoglycoside toxicity (acute renal failure and/or renal insufficiency and/or vestibular damage and/or auditory damage)
This is the **pattern of care**:
1. Use of an aminoglycoside
2. Serum creatinine not done before and after therapy (and if therapy longer than 7 days, not done at least every 7 days)
3. At least one drug level not done
Comments from round 1:
With single dose aminoglycoside in pt with short course of treatment and normal renal baseline function, probably not required.
Comments from round 2:
Same explanation

49. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure
This is the **pattern of care**:
1. History/diagnosis of congestive heart failure
2. Use of a calcium channel blocker (e.g.; diltiazem, etc.)
Comments from round 1:
Only with the calcium channel blockers with negative inotropy (e.g.; verapamil). Concomitant hypertension? Concomitant diuretics?
Comments from round 2:
Negative inotropy comment as above.

50. This **outcome** has occurred after the pattern of care below:
COPD exacerbation and/or ER visit/hospitalization due to COPD
This is the **pattern of care**:
1. Diagnosis/history of COPD
2. Use of a beta-blocker (e.g.; propranolol, etc.)
Comments from round 1:
Use of beta-agonist? Use of steroid inhaler? Selective versus non-selective beta-blocker? At what dosage of beta-blockers?
Comments from round 2:
In Aug 20, 1998 NEJM – moderate to severe COPD – beta blockers used to reduce repeat MI (? Severity and correlation beta-blocker use still ill-defined and needs more study)

The following outcomes & patterns of care were agreed to be preventable drug-related morbidities by 5 geriatric medicine expert panel members:

51. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hypoglycemia or hyperglycemia
This is the **pattern of care**:
1. Use of insulin
2. Hemoglobin A1c level not done at least every 6 months
Comments from round 1:
Apply to hyper, not hypo
A1c is more for long term control. Symptoms and home blood testing are the best way to prevent acute episodes with some references to A1c.
Tight control of diabetes can result in hypoglycemia despite the best of care.
Comments from round 2:
Home blood testing is the preventive mechanism.
Still feel that can occur no matter how diligent the care.
A1C is for long-term hyperglycemia control

52. This **outcome** has occurred after the pattern of care below:
Fall and/or hip fracture and/or other bone fracture and/or bone break
This is the **pattern of care**:
1. Use of an anticholinergic agent
Comments from round 2:
Depending on indication for anticholinergic, alternative meds may be used.
Difficult to anticipate the problem.
What anticholinergic agent?

The following outcomes & patterns of care were rejected as preventable drug-related morbidities by 4 or more geriatric medicine expert panel members:

53. This **outcome** has occurred after the pattern of care below:
Digoxin toxicity
This is the **pattern of care**:
1. Use of digoxin
2. BUN/serum creatinine not done at least every 6 months
3. Digoxin level not done at least every 6 months
Comments from round 1:
(2) not necessary in every case; (3) may not always be necessary.
Most important thing to monitor is symptomatology – anorexia, nausea, vision – if positive then do digoxin level. Creatinine indicated as a baseline test but if no reason for renal insufficiency then every 6 month checks not indicated.
Was there addition of other meds that interact with digoxin? Other chemistry labs?
Comments from round 2:
(2) & (3) the interval could be one year in most cases.
Dig level is warranted if symptomology indicates so - should warn patient of potential symptoms.
Why monitor both renal function and dig level?
As already stated by me. Agree with above comment.

54. This **outcome** has occurred after the pattern of care below:

Fall and/or hip fracture and/or other bone fracture and/or bone break

This is the **pattern of care**:

1. Use of a nitrate (e.g.; isosorbide, etc.)

Comments from round 1:

Very uncommon, other symptoms limit dosage, depends on other drugs in use. Despite the potential risk of postural changes in blood pressue the use of these agents would be indicated and a physician would continue the use of nitrates despite the potential of an adverse event.

Comments from round 2:

Uncommon occurrence, difficult to predict unless patient has aortic stenosis or HOC.

Patient must be warned against getting up quickly.

As above.

most likely required for patient use despite potential risks - i.e. necessary medication.

55. This **outcome** has occurred after the pattern of care below:

Acute renal failure and/or renal insufficiency

This is the **pattern of care**:

1. Use of allopurinol
2. BUN/serum creatinine not done at least every 6 months

Comments from round 1:

Very rare in healthy pt.

Is the incidence of renal insufficiency high enough to mandate regular testing of CR in all patients on allopurinol?

The hypersensitivity syndrome from allopurinol is very infrequent and would not expect routine BUN/creatinine monitoring

Comments from round 2:

Rare occurrence.

Allopurinol is not commonly used unless patient has high uric acid secondary to gout...you need to follow BUN/creatinine and UA level

As above.

Rare event and would not routinely monitor renal status.

Routine BUN/Cr not warranted because of rarity of the adverse outcome.

Allopurinol induced renal failure uncommon.

56. This **outcome** has occurred after the pattern of care below:

Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization due to asthma

This is the **pattern of care**:

1. Diagnosis of asthma
2. Use of theophylline
3. Drug level not done at least every 6 months

Comments from round 1:

Theophylline isn't potent enough to prevent excerbation.

Theophylline is mostly an adjunct to anti-inflammatory therapy and is used to smooth out dip in peak flow in early hours of morning. Otherwise it is not a very useful drug.

Theophylline and level is not an all-inclusive method of treatment and level is not an all-inclusive monitoring parameter.

Comments from round 2:

More importantly, is patient also taking beta-agonist and steroid inhaler?

As above.

All of the reasons recorded above.

Agree that anti-inflammatory therapy is most useful and drug levels may not clearly indicate toxicity or effectiveness of treatment.

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BIOGRAPHICAL SKETCH

Neil John MacKinnon was born on February 8, 1971 in New Glasgow, Nova Scotia, Canada. He received a Bachelor of Science degree in Pharmacy from Dalhousie University in 1993. He completed a Master of Science degree in hospital pharmacy and an advanced administrative residency at the University of Wisconsin-Madison in 1995. He has worked as a relief pharmacist in the community setting and has trained pharmacists in eight states in an infectious disease pharmaceutical care program for Simkin, a healthcare technology company based in Gainesville, FL.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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